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HNOJA87	755	105028 2	1 - 2924	15 - 2938	AL528169, AL535044, AL528170, AU131181, BE612946, BG105002, AU135757, BF056657, BG171550, BG033825, AI479941, AI355267, AU131478, AI189439, AU134843, BF667911, BF677918, BF672445, BG165663, BE079463, BE536085, AI955006, AW471118, BF244058, AV702059, BE221662, BG121124, AW382750, BF696174, AA927437, AW151212, BF107560, AU132059, AI819834, AW953778, AI609284, BF698990, AI859794, AW439324, BG030945, AU139994, BE612496, BF028646, AI206535, AA860250, AI831104, AI742145, BE813327, AW966808, AI956036, AL135266, AW367356, AL036155, BE876988, BG252879, BF126329, AI720945, AA994665, AI743900, AW993504, BE566902, AA664184, BF060653, AI687733, AA173561, BF799366, BE535901, AW379843, AI653816, AW367281, BG111300, BE567331, BE865972, BF572976, AW835282, BE694658, BF576110, BF132692, AI090217, AA629687, BF673893, AI149995, BG032487, AA081847, AU153674, BF092922, BF247055, AI299830, AI707818, BF670498, AW387918, BF675455, AU158254, AA946803, AA633514, AI147273, AA425997, BF840663, AU155668, AI276038, AI879555, AI804246, AW439334, AI567777, BF092879, BE388238, AU156261, AI880793, BF838803, AI735680, BF838796, BF793693, AI276669, AU152974, AI344762, BF840775, AI859784, AA642439, BE885399, BG170726, BE885385, AA261974, AV655055, H06260, AI095469, N31351, AI879172, AI123856, AA904011, AA400199, BF839703, AW379309, C75199, AA461594, AI150095, BF092870, BF840784, AA400360, BG170799, W45460, AI753004, W45505, BF240790, N21396, BE762409, AW862124, N27476, AA434134, AA774539, AA297332, BE762380, BF211905, BE566602, AA084443, BE702058, AI432961, AI439952, AA088269, AI039241, AA363799, AA687881, AA757780, AI149443, AA088377, AA425792, AA716770, BF092862, AI587227, BF092859, BF883837, AA666166, AI694247, AA037565, AA666252, BF922973, AW089309, AI174215, AI285541, AV697011, BE150667, H88419, BE775018, T40915, AW023229, BF840777, T83573, AA297916, AW020753, BE071395, AI186553, BF149317, AW675220, H95457, AI216872, R52751, C04099, AA363800, AI696248, AA806908, H66112, BE544848, BG015556, AI003224, H06261, C75103, H88359, BE932943, N93320, AI475318, AA298199, BE004156, AA101870, BF438939, AA298660, BE071333, R15217, BF753802, AA761472, AI572307, W25142, BF935223, AA894878, BF508277, AA297827, H66066, Z42814, AA173725, R52700, H88085, BE150666, H95456, W40496, AL535043, AA305188, AW364994, W40505, T85599, BG254457, AA516125, BG223547, AA065145, AA064868, T48493, AI300725, H88086, R78625, AW674695, C02996, AW496824, S74017, U20532, U70475, AF037350, R41655, R41655, W40502, W45509, AA032072, AA034284, AA099411, AA730470, AA954636, N86667, T10535, Z38956, AI866062, AW238674, and AW512933.

HTPGI65	756	105041 9	1 - 1942	15 - 1956	<p>BE794085, BE867150, AU139367, BG035892, BE798073, BE905298, AU134218, BE410038, BE791248, AU134164, AU133688, BE267301, BE263771, AU134441, AU136368, BF883784, AW939369, BE615551, AU133625, AI570386, BE617323, AL048426, BE901240, AA829453, AU138841, AU134497, AA773562, BF736859, AU155458, AA316446, AA526833, AA928680, AA989350, AI984236, AA856540, AU156680, AI935598, BF823301, AW374387, BF879247, AA838496, AA917642, AU154920, BF736850, AA085539, AA410796, AW630746, BE463463, AW579379, BF882778, BF883729, AI900718, AW375908, BF879765, AA524154, AW873172, BF871812, AW614779, BE185875, BE832918, AW610430, AI310958, AI923663, BF882696, AU154875, AA838036, AW841181, AU155421, AW627527, AW103093, AL523362, AU155263, AW166893, AA291982, R73021, AA535477, AW629697, C05826, AA434373, BF871737, AI079149, AW604936, AW604933, BF736876, AI350214, AA410979, AA477878, AA069015, H45108, AU157980, T78438, AA548457, AI768934, AW604915, BE873506, R50495, AA477768, AW610384, BE715674, AA433851, AA284998, AA658311, AW752319, AA327429, R53022, AW294177, AI962062, AI583114, W31277, BE049489, T27397, H12607, AI972575, BE049465, AA357493, AA573883, BF854491, T86854, AA887199, BF877001, H27939, AW780166, BF036867, AI796580, AA366722, AA159295, AA410813, R73022, AI355006, BE814771, AA159390, AI811476, R81651, AA299295, H12657, AA121219, AA366746, BF762334, AI445787, AA470893, BE068878, AA367063, AA375474, AW469397, BE001670, AI569291, AA581226, AA069080, AA369935, AW368396, AU120380, AA514641, BF209520, BF820420, AA366871, AI910605, AI363744, AI355133, AI269794, AI590047, AW964534, T30792, T78501, AA235458, R50578, H27938, AA299413, AA527542, R81448, BF763266, AU076709, AA132363, BE832780, AI453001, D25596, BF333621, AW190664, AW175766, AW793307, AW263603, AI683392, AI696755, AW518881, AI287501, AI985615, AI355010, AW192142, AA508837, AW572337, AW058307, AW572444, AI250069, AI589747, BE185617, AW474895, AI369021, BF810856, AI269797, BF804202, BF915914, AW074208, BF804203, BF333622, AW673409, BE827888, AI185429, AI798394, AI758335, AI888925, AI758947, BE962213, T11411, AA419371, AI610219, T10435, BE617806, BE827856, AW375906, AA478200, AI684039, AI744994, BE839809, BE140587, U73843, AR020776, AF017307, AX048151, U97156, U73844, AX017308, AF110184, AF016294, and AF287266.</p>
HHFGN14	757	105053 6	1 - 3333	15 - 3347	<p>BE616112, BF792009, BF311929, AI039583, AI539772, BF797018, AV652556, AI911696, BF337750, AW328182, AL039415, AV709890, BF341677, AI924929, AI024590, AI799360, AL047238, AW151199, AI610202, AI354867, AW264758, AL047276, AL047492, BF725615, AW372255, AI620267, AL048362, AW242103, AW118263, AI860374, AA576772, AA464454, BF967859, AA534442, BF967317, AL048103, AW362999, BG059706, AA394278, AA579402, AI129572, BF741330, AW150084, AA905545, AA918638, AW072583, AI445594, AI042547, AA953112, BE044458, AA614134, AI089102, BE677448, BG059650, AI270652,</p>

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HTAIN76	758	105055 3	1 - 1664	15 - 1678	BE379181, BG248320, BE394344, BE304882, BE870046, BF342593, BE869659, BE395299, BE378779, BF347272, BE867897, BE304851, BE273083, BF034604, BF528940, BF348521, BE315252, BE394405, BE869523, H11951, AL039694, AI087281, R12830, BE273008, AW800353, BE741880, BE395735, AV695990, BE871000, H58758, BE410611, AA158857, BE273259, BE764627, BE740366, BE563582, H97070, M78038, BE255407, W30987, AA377820, BG251142, BG164164, BE744662, D31501, R06968, BF569502, BF569624, H22720, W78867, BF746701, BE874990, BF529027, BE781411, BG166165, BF688742, BE383214, BE394738, BF821988, AA179431, N59613, AF016903, AX011664, M64780, AR043380, and M92657.
HL.YBO89	759	105070 2	1 - 1095	15 - 1109	AI681294, AI694310, AV733516, BE379742, BG167007, AI640172, AI074606, BG121897, AI670881, BE797790, BF940039, BE741302, BE742046, BG163770, AI858065, AI681393, BF984484, BE790111, AI400174, BF978941, BF973090, AI761953, AI910439, AI089029, BE048642, BF219348, BF670338, AI670873, BF247903, AW614075, BF245676, AV723510, AI991986, AW262850, BF542114, AW951106, AI457787, AI431584, BF213100, AV733272, BE866235, AA582224, BE293715, BE293433, BF197587, D56385, AI681691, AA459997, AA282970, AA632011, BF208865, AI769114, AA460091, AI091029, AI375169, BE958578,

					AA283060, BF677506, BF382312, AI400216, AW044700, AA782032, BE090147, BF211105, N70581, W00474, AI129124, AI909822, AI624690, AI208850, W04882, AA614862, AI799764, AI633913, AW612235, BE866291, BE972765, AA987867, AA312107, AA916363, T29090, BE503032, BE694176, AA492546, AI373064, BE762975, BF224233, AW772272, AV655130, Z30203, AW015455, AA379970, AI368642, BE772285, AW243721, R96106, AA383564, BE720406, N72193, AI868673, T64539, D45517, C20558, AI130836, AW007571, AI928680, AI191010, N87559, BE702387, BE178819, BE566653, AA834469, BF910106, BG179242, AA372905, AI963630, W21362, T65962, N67416, N93012, BF154709, BE182933, AW364315, AA248547, AW771495, AI361096, AW271309, BF111624, X72964, U82671, AF080592, AL021127, and AI025418.
HMEKJ82	760	105076 7	1 - 583	15 - 597	BG037143, BF676815, AL527704, AU125963, BF028753, AW408138, AA952954, BE782652, AV763225, U26424, U60206, U28726, AJ001529, AF271361, and Z25422.
HOFNX17	761	105096 9	1 - 669	15 - 683	BG167328, BE565189, BE789424, BF243458, BF215528, BF973004, BE738025, BF244163, BF665298, AU135381, BE738188, BE567581, BF107150, BF971769, AA129310, BF686527, BF573009, BE882050, BF685893, BE889391, AU136700, BG118456, AU139656, AU137801, BF981334, BE883571, BE885625, AU138337, AU137564, AU137423, AU135571, BE885645, BE886273, AU138129, AU139930, AU135525, BE882507, BE889674, AU138813, BE885940, BF340792, BF219314, BG117049, AU137131, AU139496, AU136839, BE395726, BE613877, BE784318, AU122831, AU139272, BE890074, BE889354, BE393571, BE019690, BF672909, BF091549, AV756671, BE890028, BE889618, BE785202, BF790680, AU135762, BE883722, BE890010, AU137370, BF672419, BE869220, AU135495, BE888097, BF673438, BF029110, AU138607, AU137127, BF972534, BF246106, BF130804, BE883891, BE566362, BE787422, BE613536, BE746626, BG164494, AU117349, BF245980, BG121662, BG121427, BF980639, AU135221, BE890043, BG111978, BF245291, BG036076, BE777467, BG119474, BE886256, BE884608, BE888717, AW950757, BE439455, BF683998, BF107275, BF696507, BE613538, AU122830, AW366472, BF107233, BF979239, BF698764, AV757833, BF349437, BG250298, BF671133, BF037244, BF700315, BF672562, BF031223, BF084959, AW366471, BE865476, BF349429, BF217501, BE567062, BE567857, BF696793, AV716650, BF218154, AW366486, BF685662, AV714843, BF243102, BF217410, BE546162, AV757230, BF680563, AV717869, BE160289, BF242795, AV756534, AW366462, BF245428, AV734845, BE160277, AV716730, AW366477, AV757969, AV755997, AV761675, AV763314, BF245840, BF209181, BF242088, N79355, BF218920, AV756589, AV713049, BF572307, BE886383, BF214785, W80546, BF692781, C18232, BF107418, AU138502, AU134300, BF241022, AA348570, BE928764, AA852087, BE565641, BF243032, BF028253, N85304, AV747314, BF149206, AV714294, AV748590, BE884043, W07418, BG010285, AA095823, AA344036, R95461, X56649, U24656, I02238, AX004164, AX004167, X95108, E01979, and E04245.
HAOSY21	762	105109	1 - 719	15 - 733	BF684581, BF342950, AW957686, AV772375, AV723295, BF237688, AV707099, BE296762,

	5			<p>BG249626, BG030540, BE904320, BE855564, BF343422, BF967357, BF381900, BE735772, AW957960, BE797433, BE795824, AA315157, AI125407, AW964045, BE857238, BF038643, BE383303, AA527168, BE877943, BG180679, AI600483, AA526476, AA524465, AF246226, BE468099, AI089960, AA446158, AI815670, AA603451, BE409219, AA541685, C14084, AA100697, BG149755, BF205057, BE856699, AI871796, AI138696, AI878833, AI185832, AI479416, AI563976, AI333816, AI141745, AW138570, AW157657, AI879393, BF750478, AW965775, AI081138, AW516945, AI660905, AI217985, D60576, AI879973, D59838, AI038860, AA102814, AA931242, BF027307, BF224241, BE265665, AA513786, AA070996, AA586819, AI096871, AV724707, BF433217, AA776763, AA125855, BF812227, BF216575, AW949359, N53018, AA682431, AA535032, BE266107, AI336049, AI356704, AW272440, AI184304, AI073583, AA306591, W19566, AA125841, AA125969, AA248470, AI056604, AI350076, AA442677, AI184964, AW297214, AI569557, AI889555, AA732059, AI301035, AA927737, AI537988, C15292, AI797215, AA306529, AA302617, AI304867, AI339315, AI149920, W95435, AA682224, AA513631, AA889266, AA429855, AI051738, BG055718, AA721039, W15344, AA947500, AA878900, AI869608, AI085201, AA552223, AA722721, AA947125, AI000301, AA548883, AA070617, AA437187, AA962818, AA129809, AA758447, AI222563, AA737832, AA991817, AA592946, AI301328, AA575968, AA779628, AA923511, W95562, D60527, AI202852, AI342761, AW192683, BE275757, C15125, BE766128, AA887528, AA938482, AW163651, BF844912, AA281870, AA991676, H64391, AA826008, AI198092, AI271711, H91874, AA281586, AA126067, H72163, C15570, AA833674, N80835, AA533218, BF986474, C15228, AA887522, D60706, AA352582, AI349428, AA317358, AV749512, AA369534, AA369535, F35247, W21262, H89937, R58065, W39436, W37085, AV737495, N20273, AA523158, AA364733, AA303269, W07566, AI349426, AA034211, N29179, BE302449, H91983, C14543, AI648551, AI925530, H72068, AI468034, D81321, N75328, AA029297, BF699753, AW862100, BF851922, AA383062, AW859230, AA431548, BE535709, AA322774, AV747190, AW859170, T93983, D60707, AA301770, AI376085, AI080573, AW859090, W04779, BE621152, AA304243, AI031902, AA878574, AA600861, AW878796, AW859632, BE206699, AA091291, AI039006, AA782434, BF435042, AA356010, BF512771, AA062921, AA375603, AI053681, BF477088, BE166757, BF183773, W24482, AF151048, AF247565, and AB047837.</p>
HMWDB39	763	105111	1 - 4711	<p>15 - 4725</p> <p>AL527816, AL533334, AL533288, AI132991, BE738228, BG034053, BE739552, BF984110, BG260492, AV755413, AW964005, BE560912, BG170764, BE891685, AW608050, BE277616, AW608063, AW608053, BF305030, BG164154, AW608056, BE069945, BF969279, AW876488, BE387593, AW386751, AW608048, BE883205, AW608054, AW373467, AW373475, AW876491, BE893625, BG032180, AL134864, AW608046, AW876498, AW373468, AW134836, AW876490, AW369558, AW836244, BG106325, AW386747, BG032622, AW373476, BG121952, AW369560, BE896621, BE566580,</p>

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HAOSZ53	764	105124 6	1 - 1325	15 - 1339	<p>           C15221, AA643562, AA2933560, AA398413, AA446482, AA452815, AA452954, AA486758, AA486770, AA486933, AA598444, AA599697, AA431474, AA722709, AA758097, AA770400, AA843343, AA843855, AA846874, AA861924, AA868908, T11105, Z30153, T16355, T63872, F00737, F10114, AA693374, AI291390, AI362774, AI367548, AI202758, AI472671, AI540703, AI540740, AI419218, AI41229, AI186851, AI651321, AI263365, AI282058, AI351923, AI633466, AI694841, AI758368, AI817250, AI818116, AI869179, AI891148, AI807302, AI928622, AI934150, AI971688, AI972172, AI982683, AW024538, AW090473, AW151332, AW263475, AW188735, AW193529, AW304152, AW469996, and AW517789.         </p> <p>           BG16754, BE742356, BG169741, BE737394, AL536737, BG035700, BF529756, AU129386, BF569781, BE906445, BE888309, AU126226, BG164594, BG112518, BG120249, BE390387, BE908319, BG104445, BE786862, BF529755, BF345037, BE272295, AU139884, BG032038, AW954508, BE385393, BF570296, BE536063, BE563539, BE886236, BE907551, BE733035, BF971649, AA292422, BF569789, BE874289, BE884694, AI346755, BG118789, AA477693, BF679397, AA526490, AI937163, AW007343, AI421549, AI186858, BG170016, BE884242, AU158211, W73114, BG163524, AW071883, AI921806, AA293715, AI677767, AA434504, AI635865, AA525971, AI245616, AI923979, AW673927, AI336339, AI982909, BF130225, AI087176, BE042450, AI566913, AW971941, AA430468, AA143240, AI042262, AI924324, AI283781, AI748862, AA405242, AL536736, W58109, AA434406, AA884449, AA477694, AA437352, AW583877, AI149950, W94126, BE150951, H30230, AI137204, BE150896, AA910258, AI569011, AI038000, AI351681, AA278265, AA505519, AA100354, BE242836, H30675, AI000002, W58219, BG261250, AA427618, AI640789, BE280007, AW965577, AI160137, AA480675, AW675091, AA402964, AI264832, BG008682, W05533, AI418798, AA143299, AI040251, AA002196, AA505527, BG107498, AA329214, N76134, AA631327, AA307966, AA864701, AA137267, H28117, AI208509, BE393546, R48090, R50206, AW080323, N31266, AI342175, R78352, AA054747, AI750670, AI620791, T66846, R26643, AA100305, T77309, AI199378, AI648478, F13345, AW583507, AA873206, AI520788, AA484092, AI625948, F36535, Z44621, T48631, AW000713, C04757, T60738, AA002067, R47978, AV707282, BF247764, T66845, H97612, AI470990, BG167362, R49672, T34246, N87910, H06178, AA514312, BF745589, AA394089, AA379308, BF247881, BF570302, AA627384, N36593, N22880, R50152, AA278732, BG014014, H90261, F30847, AU126761, BG009210, R32286, AW082510, AA054745, BF743515, AW271186, AA258044, BE925169, AW192387, AA429125, T08566, T06887, BF852854, AI567068, AI671642, BG163239, BF213477, AI263331, AI800171, BE907414, BF338002, BE622183, BF814447, AI800159, AW827276, AV758825, BF793324, BF525838, BG122101, BE880182, BE540578, BF038131, BG256592, BG032036, BF970449, BE047852, BF338723, BE876033, BF822127, BE874133, BE612681, BF529881, BE536058, BF032910, AW673679, AI273179, BG110517, AI620284,         </p>
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HSODP14	765	105125 6	1 - 629	15 - 643	<p>             AL533304, AW962800, BE969850, AU126185, BE379997, AV726266, BE782375, BF725147, AL045011, AL045003, AW996063, AV649739, BE540171, AW303509, BF382925, BG108051, F06685, AV701826, AW992687, F05888, AA371304, Z43171, BF951650,           </p>

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HPTGB84	772	105195 3	1 - 853	15 - 867	BE379478, AL519940, BE736832, AI188527, BG110885, BE737145, BF971627, BG113959, BF314524, BG109261, BF055550, BG109783, BF127747, BE786146, BG252959, AI149525, BE621303, BF795273, BF313208, BE885912, BG034281, BF307357, BE867948, AI806664, AW275083, AI061604, BE270221, AI870967, AW275075, BF971533, BG112482, BG114864, BE785489, BE546390, BE378249, AA497057, AI138600, BG054813, AW964838, AV756448, BE855445, BE536788, AI479952, AI266262, AW673935, AI185743, AA830546, BE620453, BE621749, AI802437, N28845, AI034238, AI933142, AW268994, BG165623, AI418408, BG253819, AI742943, AW956695, AI096748, BF344884, AI202120, AI147114, AA542933, AA497134, AI141476, AI1199331, BE395676, AI150814, AA410970, W79405, AA009751, AA002106, N41909, AI333142, BE857221, AA622772, AI144338, AA022637, AA808093, AA504401, W79518, AI810638, AA761599, AI417395, BG260133, AA568559, AI023970, AI095050, AI209035, AI362792, N31052, AI498037, AA846602, BE620682, AI570460, BE965683, AI161081, AI278848, AI310326, AA443683, AI075863, BE831944, AA505571, BE831950, AA419552, AI090272, AI187011, AW675097, AA594429, BG255846, AI934684, AA312223, AA143434, BE831941, AA009752, AA005006, W95427, AA345829, BF590209, AA035194, AA576272, AA954873, AA765429, AI797328, AA143435, AA005054, BF765520, AA022648, W24400, AI242550, AW150207, W24390, R01078, AI080521, AA447070, AI125782, AA429368, BE831899, AV693940, AW085314, AA157417, AA235273, H58468, BE831943, BF325592, H47561, AA384046, W95554, BE831900, AA765682, AI018452, R68502, N93667, AA459809, AA002105, AA737941, AA341512, AI018031, AA806519, BF475991, H47562, AI351234, AA968607, AA449139, BF111426, N92318, AI354927, AV743970, W24428, AI219347, AI887041, AA427981, BF838748, AA035193, AI519939, R01805, N93676, AW084368, BF359878, AA504139, AA704246, W86336, BE906008, BE810959, AA877686, AF151871, AF090922, and AC005740.
HVCCD05	773	105198 3	1 - 955	15 - 969	BE219057, AI084904, AW135444, AU139879, AI937665, N87764, AA974074, M89914, AR029030, I36272, M82814, M38106, M38107, M61213, L10370, AC004526, AC004222, D45201, M60915, D30730, M82826, M82825, D30731, M82824, U17683, M84131, U17684, AF130776, AF011748, AF031610, U17685, U17682, U35694, and U35693.
HPYSC40	774	105215 8	1 - 822	15 - 836	AA779751, AA476904, BF056494, AL047797, AA436220, AA402723, AA291495, AA293088, AI151391, AA452764, AI188355, AI086276, AA477016, AW296294, N30652, AA706816, AA436221, AA404631, AA433965, AA293479, AA235001, AA478226, AA495907, AI276581, AI246448, AI420208, AW044154, AI080180, N42277, AA252967, AI474212, AA463721, AI274168, AI092818, AA452585, AA495908, AA402883, BF446967, AA854990, T28299, BF507811, AA635664, AI420297, AI742059, AA434011, AI092114, AA405395, H52337,



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HDDMT56	775	105226 1	1 - 940	15 - 954	BE791889, AV717926, BG111059, AW026224, BE731340, AW129431, AW044302, AW044311, BF969263, AW026502, AI024363, AV764439, AV755780, AV703541, AV756180, AW005536, AV756181, AA044591, AV717648, BF698603, AA044836, BF185808, BE858602, AI884653, BE566092, BG236392, W73840, W72164, BE568051, BF446110, BG030132, BF432321, BG231607, W74588, AA584411, AA044721, BF438576, AW361071, AI359202, BE695891, BE045437, AW968454, BE857732, AW952892, AI400180, AI127248, AI361026, AI351761, W73696, AI361044, N93769, AW853077, AA188813, AI346887, AI873700, AA476929, AI564814, AI148800, BE960901, AW576052, AA844073, AI580492, AI359751, W15164, AI871309, AI159826, AI090121, AA459134, N56635, N92789, AI125882, AA936153, AA477040, AA844279, AA627857, AW026355, AI285239, AI024076, W20518, AI193641, N95574, AA130015, AI041348, AV756064, W07735, AV708855, BE728941, AA410661, AA706702, AI359593, AA722839, AW004870, AV707248, AA829863, AI202724, AI276819, AA431145, AW978868, AA432164, AW627741, AW592913, AI199842, W39004, AI193714, W39225, AA291941, BE972734, AI056225, AI344438, N80763, AA988362, AA383031, R99845, BF130957, AA445991, N78715, AA627324, AI500185, AI205678, AV653961, AA864928, AI589231, AA309919, AA293627, AA962487, AI474384, N29679, AV660336, AA130014, W24818, AV698101, AV660285, AV660175, AI077593, AV660215, BF351943, AW016040, AA651617, AA009876, C04433, BE766092, AI342842, AA747913, AA446267, C04962, AW020834, R23666, AA355416, C02690, N92536, AI561151, H56634, AI051799, AW407061, AA111947, AI420808, H99820, W07552, C05537, N24516, AI474400, AA280534, BE843719, AA315628, AA383032, AA382428, AA009528, BF740125, T80744, AA749010, N87803, BF208266, AI139832, AA085812, F26702, C05473, AA044811, N49380, T84122, AI867943, AA747825, AI687396, AA832270, AV650894, AA565864, AI083802, AI146601, AA342414, BE350230, F35829, AA731123, N49470, AV718225, H30789, AA235564, AW999222, BF242556, T89356, T80634, AV736105, AA937994, AI445396, BG165709, AV736287, AA731103, C01741, M85658, AW877209, AW979127, AL134524, AL119324, AW969680, AW975037, AW975002, AW969816, AW975031, AW972845, Z99396, AW971975, AW974801, AW979238, BF868697, AW979204, AW975876, AW969673, AW975952, AW972292, AW976024, AW975019, AW979002, AW971403, BG058418, AW975632, AW975032, AW975954, AW975965, R99846, AW974786, AW975154, AL119457, AW976023, AW971968, AW975628, BF868687, AW973717, AW974964, AW972867, AW969643, AW975027, AW979098, AJ250393, AF110775, AF161497, AJ250394, AX017873, AR066494, AX046357, AR060234, AX030435,

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HVVAV02	776	105255 3	1 - 872	15 - 886		AL537587, AL529658, AU123248, BG111713, AL536888, BF528711, AU137828, AI421201, BE904707, BE791254, BE745009, BG109317, AI570622, AI570004, AI989579, AW961469, BG108425, BF383127, BE176810, AI833038, BF696193, AW468544, AA779618, AA594978, AW009553, AI560971, BG230611, BE264327, BF589342, AA700346, BF031165, AV705472, BG119892, BE551429, AA236469, BF217607, AA975622, BE855531, AI241179, AV724761, AV705812, BE176927, AA232654, AA425074, AW304107, AI089284, BE884892, AI368096, BF697812, AI348181, BF668864, AA186811, BF817290, AI766352, R35279, AI142922, AW886555, AA584043, AA974548, AI124517, AA282137, AI400118, AW297715, AI057075, AA701672, BF154541, AI272148, AA772928, H53622, R53868, AA514023, AA531591, AA316638, AI333059, AI924107, AA641382, AW886216, AW886217, H74214, AV720966, BF060965, AI818718, AW934891, BF737115, BE833950, AI367803, N70079, H53661, AW886135, AW886133, R66643, BF737112, BE833954, BF090575, T87908, AA971632, AA703463, AI864207, AU124815, AW959681, N62470, AW888886, H16343, AW998773, H60947, F15800, AA533438, AA332062, AL039198, AA310143, AW360979, AA614390, AA621437, F11167, AI937689, AA332239, BF245833, AI538144, BF932809, AV722305, BF760088, AA665032, AA365208, AI630339, AW768928, H73698, T88002, BF760401, R20909, AI830513, BF575067, BF932781, BF887248, BE763671, AA365209, AV702237, BF760085, AV704383, AA344255, AW372989, AA363457, BE767071, BF216049, AA216158, R50400, R47763, F07468, N79190, R67362, N73190, BE242768, BF247762, BF764294, BF670200, BE695812, R20797, AW902331, AA361116, BG231332, AA234237, AW373134, AW834746, AW934899, AW888862, AW386061, AW888860, AW373135, AW373133, AW934906, BG033243, BF129853, L12387, M32886, X04656, AC005075, AL121872, AC013412, and AC003991.
HOGCS42	777	105255 7	1 - 1746	15 - 1760		AL526995, AU133713, AU122264, AU133716, AU133898, AU133901, AU121966, BE792903, AU141449, BE786350, AU133817, AU136746, BG254161, AU133578, AU133887, BE907881, AU121817, AU133655, BG260814, AU121969, AU133752, AU136516, BG179180, AU133916, BF038418, BF037422, BF036516, AU134354, BE734836, AU138430, BE873066, BE875603, AW844114, AU133630, BE616872, BE880804, AU122380, BE871117, AU134380, BE871864, BE902820, AU134369, BE536853, BG256045, BE304643, AU133618, BE787818, AA523290, AU147972, AU138507, AA700004, AI927220, AW170580, W74492, BE812430, BF446247, AU147690, BE870378, AI859845, AW935041, AI991311, AA522795, BG254485, AU136509, AI081052, AU155374, BF681403, AA535079, AU159009, AI400364, AI335984, AU147886, AU155390, AW193221, AW874638, AU155077, BE564185, AW170345, AA622540, AU155064, AI273767, AW474974, AW770097, BF445088, AW168283, AI188508, AA565989, AI559433, AI420481, AI246782, AU157642, BF182989, BF825787, AW815382,

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HPDRP02	779	105272 8	1 - 1627	15 - 1641	AI127173, BF689120, AI833019, AI299951, AW950053, AI796694, BF569958, AI207840, AA905294, AI677681, BE395678, AA595291, AA595194, AA496648, AI185277, AW514815, AI267900, AW172940, AA541745, AI672913, AI191324, AI457407, AI749865, BE612917, AA541667, AW474854, AA932637, AI459873, AA936956, BE501657, AA600983, AW008141, AI813527, AA437336, AI813526, AA427585, AW970526, BE391199, AI769112, AI188975, AA706831, AA954972, AI521390, AI812098, AW170020, AA595356, AW068546, AA976022, AW001580, AA600270, AW130267, AI587132, AI635503, N39646, AA564063, AA995165, AI750626, AI080529, AI707459, AA743928, AA599926, AA447630, AW967399, AI749142, AI371879, AA552327, AA525853, BF055306, AI038815, AI048329, AA834008, BE391165, AA541782, AI189885, AI707522, AI086832, AI436627, AI304521, AI087181, AA481901, BF725693, AI832585, AW518701, AI749608, AI076047, AI797199, AA437391, AI025561, BG118128, AI301508, AA434030, AI288407, AA534237, AI367324, AI222841,

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HMALJ21	780	105287 4	1 - 2012	15 - 2026	AL519388, BG259676, BE277678, AW205482, BE869625, BF316260, AI277584, AW664331, BE622336, AL519387, AW662197, AW136690, W52642, AI250913, AW138798, BF740532, BE677906, AW138820, AW608260, N35182, N24280, BF768395, BE144069, BE905906, AI632485, AI655964, AI350527, AI632508, AA454785, AW088958, AA351397, T79897, AI095945, AI001211, AA116116, BF948656, AI695261, AI453666, AI467878, AI368974,

HLVAR61	781	105303 7	1 - 769	15 - 783	<p>AW243613, AA928482, AI311394, AI308188, AI583510, AI023282, AA704892, C01811, AA522882, AI915997, R37609, AA116117, T39427, AI811517, AA255430, H45848, AI278218, AI090187, AW130406, AW665426, N23397, AW192328, AI094832, AI582197, BF197385, AI631532, BE672148, BE858838, AA454733, T97925, AA036929, AA180050, AA622644, H98713, AA987548, BE669564, AW368961, W51992, AK026046, AL008734, AX022320, AF131840, and AX022322.</p> <p>BE539148, AV701008, AV725116, W46534, BF208088, BF382571, BF239279, AV723526, AA156901, AV655710, AI539186, AI418461, BF590840, AW954196, BE439596, BF571987, AI697932, BF673830, AI685500, AI015531, AA442557, AI949700, BE612620, AV701346, AI690126, AI807479, AA743893, AA427395, AA706606, BE091133, AI334957, AI093104, AA634337, AI247843, BF030479, BF029431, AI150112, AI912124, AI129790, W46170, BE466890, AW300000, AI280605, N32003, AA911924, W37946, AI689978, AA428154, AA628163, BE771950, AI268698, AA970845, T47498, N26101, BE004235, H82110, AW328343, W37884, H97954, BG114369, AI935379, AW014961, T47499, BF333867, AA229994, AA303594, W05782, R24400, H82111, AW361303, AA569753, AA156856, N71934, R53408, N77889, R02637, R24401, AA878435, AW168612, R01695, T34016, N36740, AA026193, AW661659, AA026265, BE394279, AA670493, T24763, AI245496, AA090760, AA029702, AA610033, AI089660, AA994488, AA860434, AW473074, AA769881, AW891864, AI814435, AW891684, AW891868, AW827103, AI560099, BG164558, AI921248, AL513991, AL120853, AI174394, BF816037, AL513999, AI699865, BF965789, AI637584, AL041772, BF970652, AW079159, AI677796, AI824648, AL514701, AL514867, AI627988, BF856017, AL513631, AI926790, AL513597, AI433157, AI702073, BF812961, AL513907, BF856052, BF812938, AL515413, AI611743, AI610690, BF904265, AL514087, AW198090, AW167228, AL513779, AW026882, BF812960, AW148363, AV735485, AW150578, AI564719, AW983691, AL513937, AL514493, AI554218, AL514627, AL513577, AI537303, AI815232, AI889376, AI830263, AL514983, AL514721, BG108324, BF032768, AI633125, BG116387, BE886728, AW827289, AI570884, AI619502, BF970731, AI499285, AI886753, BF885000, AI620284, BE965621, AL513947, AI478123, AI073952, AI783861, AI802542, AL513553, AL045500, AL514025, AL514473, BG114104, AL038445, AL037454, AA287231, AI687362, BE620084, AL119791, AI697304, BE879906, BE011885, BG109221, AI919345, BE910373, AW073865, AW104724, AL513977, BF526020, AI687065, AL514035, AL514879, BG108288, AL514359, AI587114, AI249877, AI590530, AI494343, AV764180, AI288050, BE965121, AI567360, AL513807, BG257611, AV714485, BG180996, AW163464, AL042544, AL036274, AI536685, AW983703, AL036631, BF868489, AW102924, AL514205, AI499191, AI539153, AI311926, BE047852, BG110946, AI249497, AW193530, AW073270, AW057937, AI682971, AI819326, AW148408, AW161579, AI801325, AW235745, AW051258, BE621256, AW021373, AI610671, AL514919, AV753074,</p>
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HOVDF79	786	105336 9	1 - 2312	15 - 2326	AU119377, AI129991, BF109705, AI003504, BF970648, AI978786, AI942472, AI923428, AW157102, AI337325, AW305224, BF439855, AL043698, BE889977, AV708983, AI949346, AA779822, AW662369, AU145736, AU139589, BF336739, AA902404, AW450949, BE552252, BG054963, BE048768, AI183371, AI422983, BF478172, AI085398, AI624398, BF438641, AI743061, BE465292, BF797246, AW182966, AA653306, AA702436, AW408332, BE566450, AU145016, AW166329, AU154587, W73118, AI028580, AI088059, AW002495, AU158347, AI334137, AI432305, AI803106, AW104041, AW304421, AU158692, BE670915, AW238419, BF327057, BE253783, AU147362, AI684123, AA308483, AI034255, AI088358, AI095015, AI146768, AU149082, AI378977, AI718426, AI754081, AI002387, N51414, AI268360, AA810276, AI830449, AI151401, AU150212, AI375778, AI446077, BF115834, AI950139, AA779348, AU153375, W86275, AI088406, AI263017, AI094353, AI140293, AW803630, AU158571, W31856, AW606728, BF433824, AU159526, AI439425, AI745558, AU158090, AI057081, AU153897, AI160952, AW771340, AI248226, AA699336, AI370781, N50861, AI805789, AW080680, BE670404, AA284436, AA234679, AU157446, BF033408, AU150130, AA889342, AU149164, AA490361, AI800855, AI769864, AL043697, BF688126, BE503532, AW444986, AI266732, AW368126, AW368120, BF827396, W73138, AW873365, H82394, AW368023, AW263912, N80171, AU156841, W78224, AI803688, N34343, AA642583, R99060, AA962061, AA807778, AW772055, AA678399, AA225086, C04873, AA679450, AI783666, AI473702, AA628546, BE775239, BG059529, AA811471, AI909121, T34767, AA825759, H08335, BE178051, AA831866, AA768970, AI968631, HI17949, AA292712, T08453, T16462, W81516, AA234752, AA225217, R62711, BE177869, AA247183, AI915047, W72185, AA362699, HI17164, AW505122, AA709427, AI367965, AI367964, AW193572, R59387, Z38714, BE080939, AU118459, R44755, R99257, AA853740, R52397, AA099272, R99245, AW467886, AA480287, AW088296, T33541, T56948, AA098893, F02426, R63669, W81632, AW089041, R99049, AI933597, AI302303, W86309, AA917412, AA056449, AA301282, AW363137, AA532412, BE926640, T16601, BE844238, AW503719, AW196019, AI434011, BF082587, AI241010, AA978275, AW378894, F06155, BF733750, T35240, HI2819, AA093937, AA095746, AL118913, N56371, W70334, AI588883, AA781204, BE708492, W77820, AV702009, BF762691, BE817855, BG058239, BF089716, BF692584, AI889870, F05792, AF315592, D43951, D87078, AF315591, AF315590, and

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HOFMU50	788	105354 8	1 - 533	15 - 547	AU132452, AW291760, AI216391, AI525969, BF947708, BF337266, AK023260, AF267982, AF288992, AL121989, E17301, AB024568, AB007917, AF060178, AF169243, E17300, and D88811.
HE9MO38	789	105358 5	1 - 875	15 - 889	AA493380, AA334302, AW951691, AA313463, AA313497, BE902087, AA612692, AA321064, AW955000, BE742712, AW006877, AA299564, AI215629, BE811297, BE869635, AW242221, AI268131, BG025716, AI525357, BE875568, BE783028, BE537297, Y11484, AL136295, and X92720.
HOPJF55	790	105372 5	1 - 1158	15 - 1172	AL523613, AI583204, BG120734, BE614443, AI992172, BE886511, AI889239, AI075175, AW054762, AW471391, AI565737, AW519090, BE042738, BF732572, AI694195, AI394109, AA609929, AW167797, N30174, AI675145, AI333284, BE348940, AI348209, AW338504, AI262299, BE221339, AI140136, BE613836, AI190472, AW243822, AI142033, AA582569, AA464838, AI341876, AI357231, AA620776, AI333443, AI741278, AA865411, AA451663, AI677747, AI499958, AI292324, BF435957, W52760, AI751760, AI564037, AW297338, AI291569, AW170704, AI354944, AI498724, AI262436, AA620793, W52026, AW205638, AI247750, AW593472, AA777068, AA317293, AA582741, W03413, N46148, AA568649, AA722460, W78008, AI240599, AA923449, AA601169, BE150238, W87000, AW779522, BE812439, AA379596, AW263292, BE062962, AA379287, AA450251, AA341820, N40820, AA738207, AA853444, AW262564, H27217, C02525, AA922610, AI371985, AA359221, AW296820, AA853445, N36877, AA911932, BE693985, AW603029, AW950060, N67487, AA330786, AA581766, AA247429, AW605997, AA720994, R21859, AA341470, AW605998, R21862, AI701773, AI264461, R67787, AA992864, AI129067, W79893, AW198060, AI567586, AA857927, AI280922, R67788, N86551, AI916486, AA055177, AW580765, AI129037, BF062386, AA513284, AI149517, BE062965, AA450309, AA329559, AI971437, AI250656, AA296724, T12333, AI687174, AA091735, BF589785, AA092748, AI990853, BE077064, AA582377, AW243840, BF330684, H26201, AW603138, AX014087, U19718, AI049569, S68064, M59851, L23769, AJ009948, U19719, and AA055295.

HAOTD13	791	105374 6	1 - 994	15 - 1008	
					<p>BE799225, BE618864, BE799188, AI190314, BE902052, BE732626, BF338390, BE740450, AI148878, BE741535, BF690392, BE748721, AI081232, BE746546, BE314406, BE902235, BF316712, BE794590, AI204081, BE790602, BF975103, BE730656, BE745737, BF308298, BF969904, BF689453, AI983729, BE548414, BE618379, AA781462, BF315257, BF976258, BE745233, BG024416, BE902752, BE788069, BE255282, BE907398, AI079576, BE302855, BG118897, BE891433, BG258174, BG179007, BE255307, BE258767, AA778554, AV759912, BE540548, BE908456, AW026432, AW157348, BE748048, BG114783, AI820053, AW163407, BF975156, BE733757, BE903629, AW026229, BE905435, AI553851, AI857561, AI815796, BE733863, AI032535, BE855855, BE892753, BF797147, AA724133, BE855433, AW083250, AA412706, AA292189, BF789865, AA576423, BE353562, AA075512, BE019659, BE251323, BE019712, AI129134, AA075511, AI609823, AA551928, AA291788, AA399084, AA864673, AA399692, AA593943, AA397672, AA723613, W28583, AA310012, AI285038, AA405095, AI866592, AA774638, N22852, AW794779, AV742027, AI149026, AV717158, AA164510, AW089756, AW794764, AA886985, AI537527, AI291219, AI961557, W70096, AI015724, AA082829, AI041153, AI140036, AA725759, AA729842, R62749, AI568491, AW391249, AA287512, N58787, AW794782, AA101085, AV741366, AI290054, AI050996, AW794936, BF941032, AI692317, AW794876, BF125011, H99328, AW006955, BE300531, AI092733, W28780, BF210376, AW337357, F36786, AA076255, AI568190, AI929499, AA588108, AI929541, N91155, AW197007, AA994790, BF081605, AA971112, N35606, BF361421, AV738471, H95064, AA508023, AA287384, BE073579, BG056567, BF676892, R69908, BF674295, AI203456, AW381952, H61382, BG230794, AA477996, H48682, AW580580, AA287849, BF246820, AA481906, R23865, AW439138, AI350298, T95464, H81575, N26433, AA715821, AA367130, H70334, H94465, BF527562, AA310900, AA076254, H83767, AA917813, AA335277, AV735711, H62402, AA480101, AA747596, AI801317, AA340716, H94798, AI749929, T69061, T68984, AI953164, H61381, H48513, AW386817, AW250564, AA325135, AA336042, H93989, H83908, H96377, R78775, F19155, AA477997, BF687682, F31851, R33912, H03483, AV744024, AI458674, R92549, W16564, BF746771, BF821358, H03578, H62403, T99495, R48630, R79081, H20726, AI720532, T98906, H94558, F19427, BF738012, T19150, H98962, AW338431, BF820551, AI695819, AA317280, R22084, AI688669, H70335, R69863, BF331545, BF821444, AA304515, BF903687, R33024, N77476, AA345986, AA877573, AI871273, AX014335, X16312, M30448, AI132713, AP000504, X57152, AF129756, L15619, X52959, X56502, M98450, S56242, X56503, X80685, AF109719, AF133088, AX047063, A82595, A62298, AX047064, A62300, AR050070, A82593, AX047062, Z30183, U94592, AX009343, AX009341, AX009337, AX009335, AX009345, AX009342, AX009344, AX009340, AX009339, AX009336, AX009338, AX009334, AX040581, T95360, R22031, H00821, R92456, H93990, H94701, H94703, H96376, N71296, W01604, AA164509, AA236016, AA588428, N83194, and D20309.</p>

HODCJ32	792	105377 2	1 - 843	15 - 857	N98689, BE220444, AW014160, AI684332, AA908217, AI768199, AI420127, BE328071, AA256404, BF439620, AI268854, AI818740, AI859930, AA988651, AI240108, AI457355, AW193469, W88508, AI298653, AA705838, W90399, N66164, N64630, AA256298, AI123104, R51117, AA410637, AI565699, BE830775, AI090999, AI333934, AA321997, AI419686, N79959, AA019567, AC006160, and AB033102.
HOCPT34	793	105397 3	1 - 2343	15 - 2357	AL516637, AL536090, AU131623, AU128040, BE871627, BE887564, AI559471, BE782375, BF197393, AW300290, BF725147, AW580224, BE177290, AV726266, BG107708, AL533304, BF724858, AW771057, AU126185, BE294538, BE295415, AI033487, AL045011, AL045003, BE872512, BE350471, BE148091, AW303509, AW001892, AW962800, BF925269, BE967600, AI271904, AI863524, AA579942, BE969850, AI554943, BF951650, AV701826, BF951644, AA505945, AI424740, AA188625, BF947724, W87888, AA021522, M62015, AA451951, AV649739, AA179502, BG108051, Z43171, BE379997, AA179481, AW960727, F06685, W87815, BE934233, R74509, W20274, AW663636, AI394602, AI815234, F09307, AI263828, AA325948, BE328111, AW996063, BE503163, H24294, AW341860, AI698362, BF902323, BF889196, AI002877, T87325, AA355638, BE540171, AW379824, W21832, AW992687, F05888, BE090298, T87427, BF382925, BE095176, AI474826, AA188757, AA371304, Z42486, BE699743, BE170074, BF726249, AW510526, AA932578, BE552427, R89855, AW166687, BG178825, BF951590, BF726418, W86993, BF850658, W92023, BF842138, BE700038, BF088114, BF741571, BE958636, X81889, AC005042, U81005, D17102, and AL050364.
HFKHC64	794	105401 5	1 - 1962	15 - 1976	AL520088, AL522023, AI669758, AL520087, BF313617, BE796161, BE867541, BF969868, BE870134, BE871582, AL040779, AW007648, AU133627, AU122531, BE795892, AU118141, BE617475, BF032557, AI813416, BF984498, AI922790, BE877667, BF981072, AI818627, AI683114, BE280176, BF593818, BE262646, BE873710, BF438287, BF313170, BE867308, BF880640, AW239514, AI859453, AI805461, BF312324, BF312686, AI817269, BE798516, BE262187, AL040778, BE670555, AI589223, AI859447, BF102546, AI827343, AI088366, AI038184, AW080985, AW029180, BE313320, BF881541, AA523906, AU124748, AA404715, AA757162, AA533530, BF984274, AU126959, AI751655, W86506, BE313538, BE536712, BE873642, AI366123, AA838403, AI583599, BE796350, BE502187, BE902265, AI636646, BF915019, AA668508, AI752316, AI079121, AI752315, AW137769, W59993, BF310591, BF762496, AI677762, R59727, AI751656, AA884168, AI039262, AA729713, AA112575, BE872221, BE879109, BF317243, AA112576, R73625, AA92193, AA225005, AA128885, R73697, AA076108, T52678, AI205653, T52677, BF765650, W52739, AA159180, AI084546, AA181476, R59836, AI806402, AA159258, BF740972, AA514833, BF841749, AW178873, AU076542, AW386949, AA133108, AW953790, AW351518, AW178870, AA404588, BF880633, AA364017, AW845180, AW386948, AI818328, AW386951, AW845174, AA225050, AA182944, AI652074, C00163, AA888456, AA888545, W86439, W69936,

HOPKO37	795	105408 5	1 - 2104	15 - 2118	BF875181, D31259, BF923033, AF058448, X80038, M80206, AF044965, D26107, AF044962, AF044963, and AF044964. AL515664, AL524779, AL518207, BE797393, AL525979, BG119182, BF338628, AI978592, AW236571, AI950954, BE799316, AA976746, AI367649, BF737171, AU151637, AU151942, AW950551, AL522243, AL522244, AW291293, BF527370, AA100964, AI637966, BE906449, BF515686, AI973165, BE328566, AU150007, AI985899, BE350709, AW955183, AA903534, AL534285, N69879, AI683844, AI539699, AI862965, AA72542, AA157234, BF569979, BF928083, BF081481, AI937048, R21933, AA921357, AW263068, AW078559, R15254, BG056697, AA853109, AI921712, AA501571, AA491761, T28437, AI417310, AA974219, BF514105, AA644634, D55622, T08014, AA173338, AW239549, AI675176, AI904931, BF529133, AW887766, BF924338, BE774190, M85424, AA484169, BF854146, BF960484, BF960491, H39733, BF850364, AI363763, BF310916, R85867, AA027031, AI479546, BF081518, BE163371, AI435672, R22582, BF930534, BF849651, BE544234, AA324089, BE073147, AW949191, BF756750, BE834207, AF187148, AF187147, X59267, U00802, AL110225, D17530, and AB015042.
HNBVO53	796	105412 2	1 - 2424	15 - 2438	AU123514, BE797781, BF530408, BG110499, BG030912, BE253026, BF526281, AI655767, BG250155, BF063129, BE621171, BF348182, BE621844, AA532783, AU152557, AA936772, AW628190, BG107424, AW136709, BF344327, AU154567, AI569240, AI927300, AU152096, AU144363, BF313185, AA845914, BF476524, BE220478, AI685706, AA534332, BE779247, AW071965, AI970850, AA836622, AA121331, AA196265, N62385, AI023383, AA835031, AA309005, AI380911, AA837870, BF037753, BF929041, AI628778, BF897676, AW167088, AI635967, BE260887, AW026752, AA996092, AW591385, AA298626, AI446440, BE252176, BF815841, AA121494, AI872757, BF920701, AW948496, BF992448, AI671996, BE782229, AI359525, BE815916, N44199, BF328458, AI637865, T50194, T50139, BE314147, BF475277, AU133189, AI672561, AW880161, BF312475, BF815631, BF528463, AW364326, AW603816, BF897680, AI446734, BE730847, AL537364, BE263444, AR077146, U88153, AR077147, U88154, X75330, AL139383, AF177767, AK000250, U95739, AL022723, AF307337, AL078630, AC006944, AC010723, U72620, AC025735, AC006338, AC010088, AL353999, AC002287, AL050322, AL020995, and AW003538.
HOPKF84	797	105415 5	1 - 2008	15 - 2022	AV758100, BF980114, BF574278, BF970145, AV75858, AA628397, BF791399, AA628438, BF791467, AI743743, AA741499, AI767389, AI967956, BE380111, AV714052, AW103967, BE865483, BF208989, BE672325, AA768854, BG058541, BE564796, AV715992, AI677784, AA015599, AI765361, AW181895, BG170527, BF217259, AI811418, AA889584, AI934936, AW188257, BG109088, AI627968, AI435166, AW015219, BF217253, AI186649, BE672387, AI090415, AW967749, AI689149, BE672811, BF028345, AW301148, BF242906, BF477633, AI000120, BG112549, AA748367, AA465112, BG109521, BF894170, H81836, AA804217, AI891100, D79280, AA099034, AW016554, AA805297, AA970066, AI536041, D62658,



HCQDQ11	798	105419 6	1 - 799	15 - 813	<p>BE709427, AI698789, CI5699, AW967748, AW770219, AA211818, D79875, AA383141, BE884134, BG255002, Z36757, D62657, AI681333, AW374562, BG254237, AI337477, T34154, AI934237, CI5815, T36059, CI5707, CI4853, CI5779, H81837, BF806390, AI263154, AI117575, AF117386, AB014458, and AL117503.</p> <p>AL538129, AL525022, AI111183, BE896548, BE872112, AI174851, BE875361, BE877234, AV729201, BE880128, BE875412, BE879304, BE881218, AI133323, AI133348, BE877386, BE877647, BE881076, AV726346, AL513828, AI114736, BE879909, BE878894, AV728251, BE874647, BE878122, BE876531, AV706779, BE874520, AV705883, BE875889, BE879135, BE876719, BE881222, AV729465, BE876043, BE877496, BE898937, BE891387, BE879695, BE876425, BE877004, BE867307, BE878178, BE874747, BE870155, BE875792, BE878626, BE880711, BE877131, AV729314, BE877150, BE875858, BE877497, BE880762, BE874662, AI750078, AV706307, BE877757, AV725309, BE876651, BE877268, BE877390, BE873343, AV693283, AV705995, AV724988, BE892487, BE880690, BE873478, BE874696, AV725316, BE873954, BE879455, BE876550, BE876704, BE874926, BE879522, BE880948, BE877488, BE898560, AV702923, AI065146, BE898750, BE879410, BE874003, BE891700, BE878210, BE868527, BE881146, AL048390, BE879895, BE874445, AI110700, BE878213, BE868548, BE876098, AI147501, BE880602, BE875601, BE869133, AI749163, AV710316, BE879775, BE879302, BE870577, AI114553, BE874422, BE869149, AL036120, BE876785, AI133444, BE868532, BE899424, BE898986, AV726351, BE877242, BE897096, BE878330, AV709557, AV721544, BE897811, AV726493, AV760899, BE880425, BE880237, BE879859, BE878477, BE876062, BE867317, BE878677, BE875261, BE877643, BE896982, BE880140, BE880722, AI133486, BE868603, BE896992, BE875918, BE878900, BE875968, BE878422, AV708006, BE879413, BE895621, BE879761, AV706033, AV714977, BE875062, BE875955, BE877726, BE881506, BE880958, BE876884, BE877598, AV723290, BE543600, AI114723, AI174902, BE880977, BE881693, AV702580, BE877674, BE875438, BE873842, BE880947, BE874215, BE874402, BE876037, AV709615, BE875168, BG179400, BE878468, AV723029, BE894635, AA639334, BE880688, AI114569, AV705696, BE879688, AV723395, AV707010, AV659215, AV721627, AI721239, BE878238, AV702695, BE880276, BE877542, BE868786, AI110881, AI110734, BE878173, BE875310, BE873841, BE881638, BE881057, AV721920, AV708355, BE876568, AV725190, AI833114, AV722162, BE880950, AI114585, AV721831, BE898371, AV708529, AW583569, BE877813, BE877271, BE880442, AV723161, AV706277, AV759353, BE875398, AV722611, BE878381, AI720161, AI207615, BE895091, AV706568, BE880705, AV702323, BE877616, BE878333, BE877479, AV721391, AI133691, AI133302, BE875536, BE874084, BE881594, AI110877, AV700257, AI733732, BE880427, BE894655, BE877518, BE875382, BE881138, AV726110, BE881444, BE894924, AV721794, AV706979, AV727742, BE880157, AV648404, AR083056, I27367, X54629, AX039612, X62996, V00662, X93334, D38112, L08441, D38116, X93335, D38113, AL359334, X93347, D38114, X97707, AF134583,</p>
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HTFML39	799	105423 0	1 - 1117	15 - 1131	<p>U35430, Y10129, X84075, AX026544, AF004341, AF144745, AB005535, Z79403, Z79419, and Z79459.</p> <p>AL521566, AU132947, BE796018, BF315869, BF529521, BF342405, BG110483, BE728134, BF343720, BE730825, BE748876, BE548415, BE274864, BF339798, BF304364, BE732386, BF315441, BE786312, BF182790, BF968636, BE563888, BF038254, BG255203, BG110675, BF035338, BG119773, BG119580, BG113551, BG104944, BF793179, BE789501, BE905838, BG253457, BF206217, BG169125, BE258630, BE905033, BE78321, BG117367, BE902660, BF340314, BE788244, BE898712, BG105366, BF313550, BG249903, BE899138, BE909568, BG026799, BE621592, BG179337, BE906113, BG115754, AV721524, BE893911, BE782221, BG035773, BG028967, BE904789, BE868117, BF183186, BE728460, BG028089, BE383131, BG165408, BE385011, BG169445, BG104995, BE255596, BG115817, BF310299, BF691775, BE875197, BE877408, BE386706, BF309091, BF964982, BF669408, BE880221, BF344914, BF971354, BF315104, BE314030, BE293308, BF697543, BE256255, BF679612, BE263605, BF673819, BE277661, BG110524, BE960835, BE873914, BE313764, BF668331, BE264281, BF793965, BF665289, BG117924, AW518666, AV701703, BF793392, BE547745, BE735901, AA126478, BF982353, AV708851, BF576741, AU154376, AI140261, BG259878, BF668401, AA933701, BG164948, AA311048, AA903801, AW069876, AW950229, N25666, BF677004, AI749940, BE313988, BF968021, AA844255, BE260225, AA923066, AI190054, AW516719, BF678818, BE905919, AI189989, AA683180, AA868208, AI200522, BF700293, AI151195, BF248227, AV748753, AA618277, AV704674, BE256823, AI003622, AA928475, AI698515, AI819243, AI636813, AI873651, AV748748, AI075108, BE905993, BE786788, AI264463, AI720873, AA405732, BF312219, AA617719, AW276899, BE748286, AV752868, AV724041, H96665, AI369903, BF971263, AI984852, H37980, AA976043, AI368683, AA676347, AV763783, AA632591, AA729917, AA041378, H39510, N78663, AI185253, W07016, N95711, H38201, AW169761, AW243746, AA195473, AI874282, AI860540, AW406435, AI077646, H22238, AI281822, BG170377, AI799707, D53319, BG168389, AA152179, AA618235, N79560, W20111, H70130, R33096, BF680267, AI547083, T59878, BE907521, AI524586, H70141, H70129, W59941, H67874, AA557768, AA337055, AI027038, AI288096, AA397637, AV750982, BF525883, BF477830, AI911809, W44943, AI205865, AA404266, AI244252, BF678473, W24865, N20095, AA935411, AI186009, N22863, AI001215, H15847, AA371710, AA864565, R83778, AW079732, W46569, W46988, H70142, AA460292, AA902854, AA565961, AV695742, AI524956, BE251888, AI000752, BE408617, BF927587, AI658831, R83344, AA902531, BF917194, AA481464, AW072107, R73752, M63573, M60857, M60457, U95646, D14073, X58990, M60456, AF071225, M63553, AX024013, D28465, T59969, R33189, R70193, R80575, R82525, H16158, H25156, H25499, H30503, H64624, H82596, H96541, N20397, N25489, N31525, N39292, N42464, N71262, N71712, N75425, N80056, W25031, W39593, N90698, AA088511, AA088510, AA190403, AA190547,</p>
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HOGCR32	800	105423	1 - 195	15 - 209	D86958, and AB050017.
HFCDL60	801	105428 5 8	1 - 1145	15 - 1159	BE735923, AI797287, BG115092, BF984368, AV734956, BE782551, AW963436, BE734764, BF741486, AI417037, BE047487, AU139797, AW614852, BE206393, BE645429, AI570957, BE278325, AV685296, BG059639, AW085167, AI342088, AI091080, AI670117, BF317212, AI375955, BE727563, AA406138, AI674218, BF527302, BE260465, AI307214, AI039708, AI278555, AI308199, AI804252, BE397161, BE267961, AI143247, BE271284, AI179217, BE312935, BE857958, T60490, BE559957, AA179218, BF953246, BG248792, AA479955, BE396639, AW139810, AW800289, BE276441, BE312359, BF527732, AI290336, BF376689, BE409355, AA968854, BF819153, H81763, AW888756, AA297277, BE729397, AW800327, BE546083, AW888764, BE781522, H44302, BF12468, AA302994, T66192, R49957, N50982, F12041, BE904711, AI990689, AI990013, BF926592, AA825494, AI656978, AW025641, R59453, AA478857, AI633898, AI381847, AA234882, AW963831, AV761704, AW205263, BE397225, AA018203, BE390473, AA235309, AA298718, R50303, AA853469, BF792351, BE390003, BE561075, R50304, AA341701, BE830781, BF759397, BE296667, Z40331, AI123938, AA810959, BE908294, AI906347, AI906396, BE274582, BF028602, R47809, AA297899, AA477659, BE543777, BG122377, BE241908, BE311529, AA302955, BF767415, BF034042, BE269825, H81762, AA310733, BE276171, AW403784, AA297784, BE384715, BE968774, AA227218, AA730880, AA948131, BF819152, AI436806, AA171826, AW629605, BE409949, AA298947, AR077724, AF005038, AF295402, and AF295405.
HODEC13	802	105440 0	1 - 1587	15 - 1601	AL529027, BG032710, BF340863, AW298183, AW071103, BE280319, BE733423, AI597705, BF990521, BE295339, BE465216, BF990508, BF591357, BF990509, AA412658, W94248, AW139770, AA233003, BF305673, AI972011, AA926846, BE501013, F08452, BF205806, AI192772, AI215515, AI138422, AI360421, H85735, R19924, W67467, AI073920, AA359416, BF195137, BG250773, BE410047, BE703239, BG253012, AI971074, BF767322, AA360108, BE266899, R71864, AA628097, AA405160, AI870873, AA707220, BE799986, AI417320, AI990992, AI422884, BF061608, AI223130, W67468, AA422049, BE856683, BF063050, BE707658, AL390184, AC007059, AC006128, AB012265, and AB012266.
HUSYA18	803	105445 1	1 - 676	15 - 690	AI630915, BE315220, AI686944, AI817246, AW162565, BE748690, AA621824, AA613885, AA243477, AI148140, AA599322, BE748790, AA483552, AI096489, AA176242, BF437716, AW818628, AW818575, AA588407, AI862878, N95605, AA427425, AA412220, AW673918, AL527492, AI573043, AA470032, AA677651, AA577431, AA902530, AI434640, AI613297,

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HOCON42				

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HKMNH37	805	105455 0	1 - 1937	15 - 1951	<p>BE794712, BF056090, BG032645, AW963359, AI609324, AI797094, AU141720, BE220504, N62821, AW384434, BE391552, AI745653, AI859678, AI242676, BE869868, BG231791, AW513142, AI276266, BE018033, AI190261, N32701, AU159211, AA487433, N22994, T19397, AA574187, AA515072, AA478927, AI867978, H69438, BF903409, AI631179, AA513388, BE182286, AI004755, AW044147, H54167, AI223797, AI745295, AA657750, AA687711, AI379463, D45484, AA342547, BE673591, BE749133, AA913123, W04381, W01356, AA478809, H69850, AA769538, F34761, BE749132, N74281, AA487641, AA430663, AA461437, H54010, R72030, BE409746, BE670301, BE383720, AI625849, AA461609, F20574, F20605, BE501211, BF903844, BE390109, AW512405, BE391291, BF988687, BF998811, H83563, AW131875, AA815068, AA456482, AA436517, N40421, AW103017, BF447897, BE002531, BE276832, AA377687, BE670898, AK023923, AI390142, and AF131763.</p>
HPDWP21	806	105466 2	1 - 1301	15 - 1315	<p>BF339802, AI246593, AI310122, AI830255, BG032489, AI859560, AI817151, BE746733, AI635257, BG120662, BF304489, BF690278, AI690868, AI863434, BF307587, BG167336, AI478877, AW962457, AW370524, AI912854, AI571578, BF836273, AI597983, BE868784, AI587206, BE295076, AA745041, AI828784, BF836265, BE299440, BF344501, AI687042,</p>

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HOGCS2	807	105467 7	1 - 2631	15 - 2645	<p>AL530487, BE745421, BF530206, BE744240, BE732555, BE560832, BE728102, BE734494, BE900928, BF340173, BE899085, BG171027, BE407847, BF339012, BE391461, BE005931, BE387398, AW962475, BE392364, BF345275, BE870859, BE269190, BE280532, AA521235, AI569503, BE392132, AI530895, BE908923, BE295971, AW262804, AI264216, BE018918, BE890434, BE005979, BF961405, BF343159, BE715414, BE542338, BF792605, BE514659, AI636351, AI859499, BE675736, AI744758, AA758222, AW024550, AI126826, BF124910, AA594600, BF530317, AI567104, AI935268, AW510761, AI280100, BG149675, BG231713, AI363344, AA483476, BE245842, BE782378, BF896674, N72581, AI633705, AW082737, BF348228, AI291530, AI376854, AA862073, AA523423, AI439117, AA774640, AW360876, AA631579, BG006132, AI459751, BE504207, AW300087, AI673280, AI885032, AA405342, AA788862, BE218474, AI022088, BF896671, AA703032, AW341140, AW026262, AI168484, BE208332, BF376297, AA733166, AW574867, AA878000, AI693928, AA456364, AI377769,</p>

<p>             AI762166, BE295604, AA393265, T47288, BF995787, H80493, AW261896, AA682322, AI189548, BF338783, AA224519, BE828754, BG149772, AA398668, AW276800, BE828767, AW264368, AJ239429, C01609, N76973, BE294075, AW263725, H81411, AA813297, BG261025, BF594376, BF088543, AI362740, AW392277, BE770083, BE828760, BF309314, AW403980, R71977, AA574078, H00206, AI360375, AI949151, BE828785, BE089517, BF753501, N55486, W46600, BE828818, BG011135, BE828765, BG013533, BE828764, BE828755, AI991548, BE828784, BE828773, AA988364, AW408627, AI476154, BE828772, BE828763, BE828777, BE828813, BE828802, BE828774, BE828753, AW592301, BE828608, T58646, BE828807, BF372548, BE828817, R73494, BF359084, AW374260, BE828775, AI796868, AI948980, BE770090, BE156325, R73493, AI284200, BE828812, AI858455, BF359052, BE395483, AW316844, AA580230, AW302496, AV682937, BF510303, BE828766, BE828741, BE770069, BE828804, AW613792, D78676, BE828732, W46599, BE770079, AI089718, BF336410, BE001474, W02183, BE828816, AI420509, BF849624, BE828821, AA962198, BE828811, BE828757, AW469085, AI262650, R38776, AI857255, BE243177, BE828778, BE828801, BE828835, AI784360, BE828815, BE828803, BF376437, BF359073, AW167008, BE770068, BE770087, BE828786, R79914, BF359066, R40070, AW105212, W28668, BE828806, BE828745, BF376305, BE828783, AA468328, T31551, BE828828, BE828833, BE828822, BE770064, BE828733, BE770091, BF372547, BE770076, BE828750, BE001475, R62897, BE828752, AI198489, AA095791, R20930, BE706927, T58696, AI700843, BF372554, AJ245621, I89943, AF070636, AF109906, AL137557, U35846, AB050510, I03321, AF262032, AK000652, AL389939, AF090903, I89947, AL122049, AK026885, AL162062, AJ299431, AL117583, AK000083, D83032, AF119878, X53587, I48978, AB047904, A08913, AL137480, AK027164, AK024601, AK024538, E12747, AF130110, AL049300, A08916, AK025906, AL133014, AL133113, AF056191, AR038854, AF155221, AL133072, AL117432, A08910, I89931, A08909, AR087170, AK026504, AF113699, AL137550, X72889, AL133104, AF051325, AK026542, AF090896, AX040974, AX040958, AK027096, AF118070, I33392, AK025798, U68387, AL157431, AL157482, A08912, AF208026, AF285167, AL122110, AF100931, AK026480, AF139986, AL133080, AL133081, AF177336, AF116654, E07108, AL050116, AF138861, AL133077, AF090901, AF116602, X82434, AF119894, X62580, A08908, AK026651, AL353957, AK026551, AK026855, AL133067, AR083266, AL050024, AK026526, AK026642, AF217987, AL122098, AL133557, AF116646, AK000718, AK026464, AK026533, AK027114, AK027081, AF119875, AK025391, AK026353, AK027204, AF090900, Y14314, AF260566, U91329, AF113689, AF225424, AF119859, AL359601, E08631, AL133016, AF130082, AK026600, AB050410, AF146568, AF271350, AF130104, E07361, AL353625, AF132205, X70685, AB047941, U58996, AX020124, AF242189, AK025484, I48979, AF081195, AF130066, AF218031, AF116610, AK000137, AF130099, AF057300, AF057299, AL050277, AL122123, AR038969,           </p>					
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HTEHP29	813	105517 4	1 - 875	15 - 889	BG110560, AI631281, AI625779, AA195347, AA195272, AW474711, AI265934, AI138775, AW016790, BG116032, AA884056, BE378635, AW594221, AW117655, AA813932, BE501702, BF970724, AA523692, AI612804, W15522, AI269236, AI688937, BE048861, AW269485, AW269486, AW269484, AI004948, AI038706, AI889700, AI470952, AA812584, AI160543, AI285978, BF221831, AW771552, AA557400, BE502099, AW516672, N23668, AI888851, N22625, AA700480, AI204356, AI381560, AA161383, AW439318, AW299589, BG236353, AA700153, AW273361, AW303803, N59616, AW769118, AA007426, AW243227, AI302000, AI189245, AA195140, H63951, AI480339, AA404683, AA044991, AA515881, AI073466, AI825630, AW271843, AI971564, AA195346, BE090990, AI699944, AI033808, AI873005, AW263931, AA634226, AW337201, R91419, T98768, T97607, AV647493, W15411, AA579985, AW341132, AW970838, BE540541, BE169724, BE673623, BE163714, BF849453, AA732611, BF326748, AA348483, AU125299, N67124, BE178033, BE169478, D20935, AI554244, BE842937, AI824259, AA156037, AA156188, R29401, AW370209,

HNOJJ32	814	105524 8	1 - 2409	15 - 2423	<p>AU117466, BF591713, D82494, BE503984, AI933783, DI3644, AK025831, and AL137760.</p> <p>AL534390, AU119754, AL534391, BG166638, BF435674, BG167871, AI796967, BF795015, BE644847, BF681391, BF448215, BF435801, AW195747, AI142105, AU148848, BF431958, BF590714, AU146016, AV707400, BF850758, AI740869, AA191594, BF943026, AI498701, N64011, AI948435, AI191083, AI125704, W86389, W86388, BE047729, BE047722, AW673294, BG055851, AI282275, AA887501, D61002, AI197956, H80459, BF095155, AA330746, AW204689, AI003139, AA219621, AL046187, AI985257, BE889906, H99275, H81379, AA346169, BE140220, H05031, AL046188, R20553, AI912734, T30719, R41899, BF062269, AI197904, BF377757, AU133106, AU154500, BF349751, BF736129, AW386705, AA779217, T24891, BF380122, AW960899, H05030, AI864073, AW841797, AW895025, AA992514, C00222, BF090602, R17531, AA338366, R12654, BE903088, AW020592, AW963756, AW945168, AW950267, AI568293, AV750565, AI525653, AW020397, AI541321, AI263584, AI499570, AV660096, BG253033, AW023884, AW020634, AW949477, AV702794, AW955902, AW954384, AW023863, AW952414, AW021178, AW963879, AW961253, AW965840, AW963028, AW950220, AV688667, AW022826, AW963490, AW958647, AV654896, AW953930, AV685966, AV709869, AW963915, AV690007, AW953657, AV728806, AI538564, AW950223, AW954031, AW949453, AW952439, AV727990, AW950247, AV722222, AV702932, AV702026, AV705341, AV707024, AV701620, AV707296, AV707767, AV704182, AV697638, AV729462, AV703472, AW019988, AI522052, AW023351, AW020931, AW020328, AI636727, AI871660, AW004606, AI884318, AI633125, AW022308, AI579901, AW152182, AW020425, N25033, AW950438, BF811804, BF766531, AW021693, BF669151, AW022299, AW022981, AW020406, AI557238, AV753074, AW966420, AW021182, BG122005, AI701097, AA282824, AW953967, AI935799, AW960594, AW949931, AW953787, AV696791, AW952457, AI557808, AI887381, AI909697, AW961037, AW957058, AW023469, BF247298, AV687527, AV686414, AW965144, AV728592, AV683272, AV683443, AW951618, AW955082, AV708834, AW953974, AV686346, AV655425, AW960622, AV651436, AI283760, AV646347, AV725055, AV660773, AW959837, AV683513, AW961388, AV703222, AV703168, AW955447, AK021892, U06944, AF218031, AX015915, AF122922, AL117587, AF273680, AK000418, A77033, A77035, AL080139, AF267849, L35261, AF130056, X95310, A52184, AR038854, AK027052, AL136623, AL389982, AL117416, AK000414, AK025435, AK027209, AF124728, AL137292, AF232009, AF082075, A44314, Z13966, AF200464, AK026762, AB040710, AF060555, AF124396, I32738, AL161628, and X82397.</p>
HFPHF52	815	105530 4	1 - 2758	15 - 2772	<p>AU130348, AA203203, AU137741, AU118352, AU139258, AV704315, Z78344, AV753316, AA033956, BF514743, AV703009, BF959037, AA460030, BF959893, R68616, W01743, BF962431, AV721634, H08927, AA065274, AV695644, R0946, R07050, N92694, AA328671,</p>

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HBNMF62	816	105538 1	1 - 846	15 - 860		AL537976, AW956448, H07075, AA324184, AL520712, BE741654, AL524606, BG033728, BE794207, BF348472, R87835, AA378653, BF313918, AL537255, BE267461, BE267321, BF912788, W27716, AA136431, AU119617, AL133100, AK000538, and AK001070.
HTPHO72	817	105542 6	1 - 1804	15 - 1818		AL515354, AL535230, AI344225, AL515353, AL536975, AL535399, AL533863, AI654097, AI935237, AU142576, AI016651, BE910134, BE872446, BG260941, AU143745, AL535398, BE439406, BG115401, BG034018, BG027510, BE782872, BF695570, BG260932, AI762092, W51807, BE146116, BF694327, BG253458, BE779739, AW893944, AU129145, BF698576, BF700754, BF573679, BF129881, AI970194, BF665235, AW611571, BF591202, BE706104, BE567334, BF433874, BE146266, BE146334, AL040782, BF571654, BE961109, BF213184, AV711990, BF666541, AI434757, AI809575, AU151324, BF436559, BF941072, BF666197, BF572918, AI380628, BE877752, AI765338, AW780337, BE866436, AI860828, N35551, AI312100, AI888850, AU160791, N38846, AU159863, AW131269, BG029915, AL120373, BE047581, AI184923, AA176692, AI683921, AA174146, AA412655, BE501002, AW898306, AI347273, AI276633, AW102943, N26499, AI422695, BF130425, AA588551, BE503660, BE208291, AA226075, AI827056, BF875808, AA130382, AW439736, AW264891, AI365107, AI992306, AI148231, AA984929, AI148984, AW150079, AI832181, BF209487, AA854340, AI038905, AI269468, AI769880, D44928, AI863221, BF941118, BF132158, BF955433, AI125729, N39373, AA598676, BF208879, W74515, W74727, AW168399, BF038829, AA835921, AA471029, AA412541, AA121750, AA225920, H45060, N38937, BE146178, AV714470, R59338, AA984875, BE090546, AI587527, BE156359, R66182, AA877664, C03753, AA503281, BG009124, AW768657, AW975255, AI270523, N71517, AI583706, AI475197, AA121696, H03152, N90562, AA664776, H40657, AA171666, H87950, BE221773, AW841003, H22889, AW069437, D29581, AA345955, H03959, T07680, T29262, H27853, N29944, AA334350, HI3366, AA298274, AI865965, AW951202, T30144, C02396, BF336094, BE928330, AA328738, AI863521, AI375079, BF688070, AI572168, BE697724, R79702, AA169304, AA709200, R72957, AA420636, AI933880, F09514, H06035, AA169629, BE697960, R67062, AW190063, N22142, N71849, R59337, AA333367, AW379738, H88342, N79599, AA318557, N46507, AA435823, BF093500, AA397882, AI049760, AA810637, AI857295, AW150981, BE176219, AW150797, W31502, BE697727, BE901570, BE176161, Z39877, F10482, R63552, AI003042, AA171671, BF810987, AI905110, AW168890, AI123901, W19066, BE816131, W20205, AW893945, AW893929, BF965877, T25159, BF438299, BE730723, D81615, AI634225, BF977281, BE280037, H45029, BE697716, AA664611, AA213866, AI247193, AI590830, AI633419, AI681985, BG256090, AI288285, AI554821, AW983754, BF792961, BF925729, X78669, AR048126, AR087768, U15734,



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HOPKL18	818	105543 9	1 - 2280	15 - 2294	AF1761713, AI188464, AI148549, AI189375, AI057119, AI857728, AI189469, AI123521, AI160647, AW301093, AW131758, AW170213, BG104963, AI184253, AL048485, AI435827, AI743911, BF475827, AI983673, AI183288, AI189903, AI743259, AI911896, AI221537, BE676513, AI700325, AI221066, BF312132, AW167259, AI768353, AI199933, AI452807, AA864277, AA453073, AI209179, AI220687, AI743248, BF432034, AI741318, AA429293, AA479583, AI819317, AI167955, BG149848, AI951614, BG005361, AI367783, BE151673,

AA291436, A1741606, A1815190, A1539339, A1285083, A1446262, AW804548, BG005385, A1138212, A1922796, A1075934, A1191884, BG005360, A1160583, AA954935, A1678007, A1336048, AA446113, AA290586, AA516357, A1160501, AA425017, AA291560, A1189820, A1126136, BG011539, AA401885, AA938118, AA568702, A1831216, A1159990, A1373695, A1126390, A1189456, A1081329, A1184743, W07759, A1742579, BF111856, A1015193, A1740764, A1199857, AA948117, A1923616, A1874229, A1147159, AA131838, AW130167, A1831596, A1653762, A1122961, AA452905, A1393898, AA291880, A1188369, AA477422, AW301104, A1587393, AA131750, A1220843, BF439872, A1000847, AA040568, A1189365, N98503, AA426599, AA535139, A1149011, AA936568, T57909, BF871323, AA455196, AA470667, A1674139, N30095, A1142786, N30252, AA446418, AA058889, A1220806, A1206067, A1571842, BG231229, A1138459, N40886, A1400681, R63721, AA872229, T54425, AA213656, AA778047, N30901, R76983, W15369, BF848576, A1955521, R83035, A1864627, AW168063, W31069, A1220657, H12886, T54473, R27372, R26121, AW103348, R27373, N57149, AA748894, W86784, BG011532, AA080417, H12806, R73809, H00626, A1680313, R73952, BG009595, R28385, H12763, A1493875, H03758, A1265936, R28625, H00397, AW190420, AA027995, H03895, A1192311, H12709, R69308, BG015954, AA454855, A1126404, A1188586, W39400, R82781, AA464448, AA721111, H12731, AA457093, A1554159, H12708, R73810, H01636, R75955, H03842, N80698, N32141, H00333, A1220728, R63768, H28432, A1609946, R69309, R69323, N56767, AA393343, A1961248, R71037, A1213709, H03843, N31621, AA033690, R94440, H02862, A1039120, H02280, R26333, H12732, R23368, R35443, A1337465, T29054, R76791, H03622, H00396, BE042740, R80919, R24178, H00295, R26852, R26729, R68071, R28505, AA524002, R27250, BF732295, H03621, R31049, R21807, A1860617, R80201, BF696299, A1219082, A1223074, H03894, T57992, R78980, R80920, R71038, I17126, X57766, Z12604, I17127, AF0000349, AX017301, U46034, M31126, X63162, X84664, AF026008, I33392, Z13966, AL355719, AF113699, AK027129, AF155221, AL050138, E06743, AL389935, AL133049, AF155148, AF078844, AX040958, AL137523, AX040974, AF195092, AL137530, AR083266, I89947, I48978, A77033, A77035, AL122121, L04849, L04852, AL353956, AX046716, AL080154, Z97214, AR038854, AL122045, A93350, AX010492, I32738, AL137478, AK026057, AB049892, AK000618, I33391, AK026647, AL1355701, AL050155, A18777, AC004878, Y11587, AB050431, AL137256, AL137480, U75932, AK024588, AX005848, AF141289, AF113222, AX005804, AF044323, AL050092, AR038698, AF100931, A65341, AK026749, I00734, AL133070, AK000653, AF285167, AB034821, AF002985, AF067728, AX042059, AK000137, AF200464, AK024622, AK026630, AB044547, I29004, AL357195, AL117587, AF061943, AK027144, AF118092, U80742, AX020124, AL133637, AK024747, AL390184, AK025113, A45787, X79812, S82852, AX014095, AK027160, AF130099, AL359620, AL133619, A08910, X66417, AK026462, AK026542, A08909, AR013797, AK027161, A08913, AF183393, U30290, S77771,

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HBAAE59	819	105544 6	1 - 885	15 - 899	<p>AA890595, AL036333, AI040915, AW007541, AV721272, BF439791, AW959421, AW083887, AI654275, AV722199, AA808896, AI800095, BF438031, AI355440, AI799635, AW604976, AA576448, AW006257, AA630283, AI559991, BG179455, AA743625, AI652663, AA151139, AI144203, AA604807, AI984722, AA194391, AI589272, AI755275, AI271562, AI560118, BF822480, AA151140, AW302262, AI167873, AI332444, AI801686, AA594332, AI148030, AI142313, AI090644, AI803537, AI373476, AI336084, AA554043, AU146489, AW022283, H29466, AI049688, AI041568, BE902412, BE328300, BF593596, BF822451, AV722821, AV682616, AA492300, AW193739, R42909, AA442117, AI285963, BF941682, AA081057, AV764612, BF839445, BF821831, H50360, N26936, AI872953, N66716, AI991792, T52344, AL036332, W95685, H91241, H68058, BE326879, AA928951, BE929039, BF734080, AI765685, AI536035, AA504565, AV722859, AA505844, BF845220, AA355104, T23042, F04483, D45524, H61892, AI003120, AI933999, AA989528, BF884269, BE843668, BF093624, H92604, AI470441, F08851, H50770, AA480590, AI468163, AA969568, AA612865, AA280393, AA632042, AI090330, AW894028, T52417, AW339041, AA301168, BE717578, AW845069, AW845073, AI905180, BF923457, H92264, AI905146, AI905179, AF091264, AF042857, AF069517, U50839, AC004814, and AJ006486.</p>
HTXKD84	820	105546 7	1 - 1833	15 - 1847	<p>AL535115, AL535435, AL527788, AL528128, AL522629, AW964128, AL530568, BF690299, AI927433, AU143450, AU122604, AU120010, AL513898, AL528273, AU124013, AU117741, AL525487, BE512822, BE799364, AI929021, BF312371, BE747909, BE868722, BE622350, BE901551, AU134818, BG257575, BE278821, AU134124, BE278080, AU135723, BE903064, AW248980, BE267190, BF689756, BG248738, AW966750, AV722010, AA723729, BF002408, BE794373, BG168135, BE273143, BG029684, BE544741, AA573842, BE293074, BE264692, AW073760, BE869623, AA908776, AW955340, AW953331, AW629302, AW170127, BF591127, BG120515, BE883708, BE884952, BF219684, BE548925, BF678527, AA456271, BE773056, AW249233, BE267954, AI360166, AU117779, BE262787, AI363345, BE167602, BE888509, BE298528, BG058608, BG117800, BE257040, BG113720, AW247642,</p>

<p>             AI129555, AW161324, AA307913, BE207113, BF696984, BF309175, BF923467, AW028802, AA775258, AW402674, AI214455, BF215524, AI225130, AW747919, AA479651, AI453640, AW166252, BF347719, AI273604, AA427606, AA578575, AA643586, AI795792, BF675073, BF348220, AI651442, AI114673, BE263421, AA427797, AI351019, AA829824, AV702563, N25004, AU130147, AA351088, BF673214, BF237597, AV735815, BE247371, AW370507, AA234404, AW732966, AA931586, AA351758, BE799206, AI671719, AA722657, AA349419, AW370512, AW615529, AA323043, N54042, AW391273, BF972494, AA299249, AA305449, AA336472, AV660463, BF448384, AW008934, AA446368, AW150988, AA913572, AW407109, AA142880, BF815623, AI805168, AA934989, AA524402, AW272469, D30947, AV692278, AW593057, AA357535, BF807009, BE777795, AV749311, AV659906, AV696695, AA325708, BG009422, AV685149, AV687812, AV697183, W21221, AA378140, AW674928, R34201, BF571081, BF675326, BF868616, H54121, AA282751, AA373758, AA351810, AV687976, BF572318, BF089571, AA322736, R19680, F08579, BE771944, BF756567, AA330657, W28070, R20314, BF953820, AA852676, T97256, BF476887, R35844, R20313, AW391794, BF089622, R20311, R34318, T27059, AA693330, T27057, AA877715, AA609395, BF895339, T97367, BG114219, BE720775, AA988726, AA299139, BF908899, AA425727, AA911461, R18854, AV747739, BF895340, BE940678, BF940145, BF895336, AW882102, BE940675, AW845077, AW794735, BF747446, E12643, U89505, U89506, AL050172, X94344, AK025484, AF087943, I89947, AL050024, I48978, Z97214, AF155827, Y16645, AB052191, AL049283, AL110225, X06146, AF031147, AL137459, AK026959, AL122098, AK024538, AF143723, AK027114, E02221, AK026480, AL359583, AK027200, AF017152, AL096744, S68736, AF119875, AF116654, AF116631, AF090900, X66862, AL137538, AF106862, AL050277, AF119894, AK026631, U68387, AK026534, AF067790, AK025414, D16301, AK025798, AF026124, AL137529, AF177401, AF175983, I48979, AL137429, AL137550, AL157482, A12297, AK026624, AR013797, AK026744, A08913, AF113019, AR068753, A08916, AK025092, A005690, AF090943, AF177336, AK027182, AK026927, AL023657, AK000083, AL049382, AF113222, AX020124, I09499, AL137488, AL050393, AF116698, U88966, AF155148, AF210052, AF079763, AL117648, AF180525, A86558, A65341, AF202636, AF061795, AF151685, AF260436, AF106657, AL389935, AK026647, AF119878, AF218014, AL133081, AR070212, AF116646, M27260, AL442082, A08912, AL389982, AL122110, AK026533, AF116688, AK026855, AF113689, AF119899, AF065135, AL137478, AB047941, AF119909, AK026613, AX045159, AF130099, AL050116, AL359620, S78214, AF130110, S61953, A18777, AL353957, AK000074, E01614, E13364, AR038854, AR034821, AB048974, AK027160, U00686, AL162002, AX040958, AX019230, AK024588, AK027096, AL110196, AK026057, AX017991, AX040974, E07108, AF260566, AL133072, A08910, AK025541, AF130082, I89931, A08909, AL359622, AB041801, AL050108, AK000486, AK026600, AF207829, AK024992, A65340, AL122050, AF119865,           </p>					
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HTXRR82	821	105548 0	1 - 1663	15 - 1677	AL525841, AL528084, AL523788, AL530647, AL528085, AL530205, AL525887, AL523789, AL530206, AL530648, AL530020, A1741904, BG111251, BE783284, BE304619, AW246206, BE409176, BE797194, AW249939, BE896428, AA631248, BF837752, AL262225, A1076571, A1379987, BF760075, BE791843, AA747742, AW182741, A1039409, BE791484, BE898142, BE171695, BG008706, AL266555, A1470348, BF351795, R08484, AA316496, BE246277, BE243727, AA628030, AA034425, BF842855, BE243741, AA053916, BE273715, and AK026518.
HAIBU62	822	105558 2	1 - 2394	15 - 2408	AW960778, BF670863, A1891069, A1760315, A1658836, A1802396, AUI45031, AUI47448, AA857432, A1564713, AA191075, BE180121, AW007299, A1082050, AA923198, AA581379, AA228040, A1383961, R45310, A1828459, AA228150, A1655170, AA227869, AA292098, AUI21676, H29021, BF733569, AUI18481, AA191665, BE706359, H13408, AA291928, AA954433, H29122, AA345806, R20228, AA337411, BE465193, BE561996, R43321, Z41361, AA748172, A1915244, AA730958, AW381210, BF508602, A1017072, AA227488, A1784588, A1913410, AA960809, H06070, AV745980, W20232, BF671807, AA634199, AA362928, AFI48848, AF076249, AK021646, AF155508, and AL133070.
HDTAY29	823	105563 2	1 - 1296	15 - 1310	A1655115, AW969080, AW340416, A1088414, BG168598, AUI133786, A1766935, AW955824, AA432162, A1243534, A1355372, BF813174, AW340370, AA01958, AA127678, AA001942, AA121541, BE089820, BE089818, AA149985, AW996875, BF514913, A1806604, AL048412, BF663006, AA431143, BG167354, A1784544, BE005808, BE178989, A1219527, BE178950, BE005809, AA136529, BE172359, BF799552, BE178947, BE005724, AUI44539, BE178953, AA026727, N39996, BF665736, BF184492, A1982645, BF246646, BE005719, BE005823, A1806323, BE005602, BE005615, BE005617, AA026615, BE089808, BE005616, AA992408, AW593294, AA993913, AW629540, BG036581, BF665789, AA043644, AA504274, A1863566, AA916510, AA904815, BF438331, BE765047, A1968518, AW629858, AA831295, AA152142, Z28590, AW378121, BF915893, Z19353, AW607533, AW999039, N27265.

HCOQD79	824	105576 7	1 - 1192	15 - 1206	AW510968, BF973883, BE766024, AW999704, AA525208, BE939841, AI651184, AW606060, AA001335, N83663, AA001281, BE005677, AW999551, AA897151, BE005649, AA029860, BE868845, AW582793, BE005713, AA136752, AA332736, AF245356, AF245357, AR093962, AJ250865, AF260225, AC073130, AL050162, AK021575, X78989, and X78990. AL521552, AL521553, BE799414, BE796064, BF569290, BF057457, BE259781, BG031400, BG029406, AW246213, BE272289, AI991822, BG031562, BE794799, BE740782, AW005567, BE266149, BF568283, AI760253, AA552351, BE744611, BF316077, BE745416, BF796423, BE906148, BF569309, BE731561, AU14985, AW246651, BE728637, AW150853, AI144315, BE747742, BE745668, BE208604, AU118415, AA917665, BG028996, BF342097, AA847227, AI811247, BE047940, BF001891, AI056428, AW276233, BF568258, BG167035, BE742415, AA445958, BE393329, BF972798, AW027429, AI863189, BE892428, AI198367, AI480232, AI041893, AW083270, AA488920, BG176928, BE273932, AA430213, BG179522, BG104852, AI342849, AA568169, BF314050, BE264597, AA516013, BE741159, BE514797, AA946875, BE263994, AI032102, AU156180, AA662705, AA427415, F28974, AA604545, AA113999, BF939307, AW962896, AI971135, BF971760, W92520, BE514803, AW050759, AI749378, AA676954, AA113998, T80366, AW078903, AW075249, R73441, AA903416, H17946, AA488849, AI866021, R51976, F19320, AA300068, R73442, BE743046, AA703568, AA371201, BF439443, BE645932, AW406525, AI186416, BE267243, AA411354, BE728187, N99524, AA427414, BG032561, AA687478, N71680, BE512695, AW246412, AI198472, AA349876, BE885663, AA411732, AW793163, AA527471, R53313, AA913234, N99453, AW087551, AA494167, AA468418, AA825644, AI345370, AK001023, AL031724, AF118394, AF114169, AF220294, Z36821, AL031718, AJ012582, U68233, I92592, A27631, and AF035305.
HAMHN12	825	105589 9	1 - 1785	15 - 1799	BF526465, AW026325, BE542706, BE542707, BE855427, BF196774, AA864639, AI287672, AI885416, AI424243, BE855854, AW577426, BE858918, AI276664, AI342436, AI420272, AI298488, AW602166, AI732365, W79647, BF389550, BF437295, AA889422, BE677567, AI420762, AA228426, AI686213, AA224927, AW339154, AI146289, H93603, AA574391, AA228353, H05698, AA694242, AA224998, AW629590, AI000160, H93602, AW613178, AA631694, N90717, AA256985, W74079, AA256986, H27807, AA639700, AA781512, AI247191, BE856659, AA256485, AA333630, AI468186, R83652, H44430, C01115, AI380982, R83651, AI350743, AW577102, AA256868, BE817585, AI674835, BF330948, BF330943, AJ400877, AJ400878, and AF086390.
HODIY67	826	105600 0	1 - 4308	15 - 4322	AL524194, AU133020, AU118936, AL524193, AU119223, AU123242, AU121697, AI961260, AU133891, AU139520, AV710009, AV728811, AI335254, AW163596, AU127807, BG164222, BE886798, BG028956, AI798785, AI650480, BE932104, AA311103, BE541225, AV694234, BE780965, BE220832, AI040228, BF197063, BF434796, AW162882, W05746, AI267777, AW965426, AW386260, BF509507, AI768758, BF110042, AA746489, BE645065,

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HNTR57	827	105609 7	1 - 1585	15 - 1599	AL537894, BG258704, BE047764, BE868736, BF340077, AI801416, AI762850, BF434262, AI742931, BF439373, BE644804, AI138559, AI797233, AW188187, AI380612, AI522102, AA868281, AL043757, AA426266, AW473173, BE645012, AI016269, BE207382, AI950202, AA910365, BF115501, AW051847, AA453144, AI263901, BF590758, AA425975, AW662298, BE281125, AW673734, BF512736, AW025120, BE645067, AI866541, AW299359, AA410629, AW263141, AI801012, AI472095, AI127189, AI088811, AW571861, AA836887, AW516893, AA502586, BF439167, AA676768, N92308, AI038102, AI632072, AA875868, AW516321, AA902731, AI274022, BE138815, BF125686, AA863331, AI721215, AI963518, AI468226, AA235644, AW969404, AA161034, F27866, AI910725, AW000879, AA741323, AI289063, AI354994, AI139962, AW104375, AW194619, AW614642, AI537733, AW169223, AI990330, BF437477, AA554004, AA973055, AI673688, AA291376, AA460182, AA410817, T73725, AI940057, AA403305, BF745263, AI940055, AI940052, T73700, AI142749, AW614314, AI918714, AI364787, AI985850, AW340231, AW080372, AI749845, AV747392, AI686667, AI814114, BF746001, AA902525, W24702, AL048891, AA758059, F37331, BF745253, and AW372234.
HUKFL74	828	105610 2	1 - 2429	15 - 2443	BE796779, BF314720, BE296316, BE311402, BF206459, BF313266, AW245438, AL134658, BE728308, AI991631, BE294807, AI991255, BG111031, AW001543, AW245796, AI830089,

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HTEBF05	829	105610 4	1 - 767	15 - 781	<p>AW340840, AW519058, AW161869, AI887324, AI885451, AI040985, AA405326, AA159189, AI612812, AA657959, AA298813, AV702726, AW963931, AV705545, AV661866, AV726708, AV705217, C15737, AW963940, AW954129, AW954735, AI557264, AV702189, AV696302, AV726916, AV702878, AV706278, AV725294, AW961666, AW951516, AW954772, AW963397, AW963117, AV703593, AV702148, U53476, D83175, AX027923, M89801, M89802, and A84916.</p>
HOPKD19	830	105627 5	1 - 1454	15 - 1468	<p>AL514608, AL528469, AL528936, BE746015, AL521772, BF690094, BE790826, BE790935, AL518173, AL515593, AL518172, BE742331, AI91053, BE729223, BF530756, BF312746, BE792243, BE901574, AL515819, BF664201, BE795515, BE900232, BE887232, BF303634, BE535191, BE729997, BG177383, BG248306, AL529609, BE544736, BG106483, AA826340, BF982191, BG253167, AL515592, BF982788, BF525820, BG108991, BE728913, BF974236, BF528108, BG031382, BG031585, BE777805, BG121579, BE264024, BG167191, BE791853, BE378819, BF797508, BE549254, BF980530, BF797481, BE778043, BG028063, BE745313, BE563774, BE782976, BF794209, AI625492, BE909865, BF345302, BE543174, BG250283, BG250199, BE544765, BE379191, BE543875, AI434163, BE778018, AI188794, BF309788, BE545242, BG117942, BG110383, BE251838, BE898982, BF308052, BE409243, AI986077, BE545315, BE389907, BG117495, AW001257, AI499406, BE275460, AL514607, BF314282, BE276384, BE383327, BG259890, BE389361, AI608736, BG115641, BF237552, BE536648, BF315248, BE548410, BE277397, BE389020, BE304445, BE255993, BE734099, BG112690, AW172971, BE544670, AI609082, BE900812, BE784989, BG027636, BE744256, AI624012, BF128698, BE257241, BF316397, BG258382, AW575251, BF307121, AI735180, BE535951, AW575944, BE382554, AW572325, BF439251, BF337954, AL515818, BG025498, BF526215, AW951827, AI818207, BE388264, AV702179, BE389281, BE222313, BE276340,</p>



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HISBE12	832	105637 6	1 - 2587	15 - 2601	AU113356, AU134630, AU137852, BF672805, AU138245, AW953092, BF574374, BE069938, AA418061, BF126477, AV704855, AV733475, AA490669, AI126748, AW021070, BF107314, AW169111, AA044844, BF432458, AW963336, AA917826, AI859443, AA402341, AA134033, AA772171, AW261848, AI979109, AA411838, AA827550, AA993572, AA490670, AI689396, AI564514, AI589042, AI962882, AI951442, AI457657, AI274779, AI126270, AI859726, AA846743, AW139081, AU155829, AI887980, AI560718, AI131563, AI160023, AW139075, AI244973, AI288216, AW167802, AA449011, AI092410, N71091, W23461, AA001805, AA024894, AA771989, AI332470, AI362305, AW022540, AW129473, AI357333, AI524525, N40765, BF106969, AI276660, W72460, AA099736, N70641, AA417957, AU157537, AA563938, AI355584, AA860530, AI734946, AI344521, AI185811, AA954648, AU155547, AW166786, AI028138, AI276661, AW771189, AU157338, AW419084, AA452645, AW168035, N90530, AI801066, AA983225, AI041476, AI424177, AW152395, AW189459, AI344395, AI015682, AI127313, W76518, AW014696, W05460, AI266450, AI689224, AW515862, AI016555, AI298435, AW024736, AI569566, AI095864, AI475928, AA614454, AI539532, AI630231, AA056733, AW591105, AI874113, AA133968, AA934658, AW474609, D82422, AI031797, AW513075, AW129011, AA099737, N40768, AI579994, AW150847, AA058387, N22767, AI690491, AA226177, AA226521, AI299561, AW518280, AA781624, AI138761, AI680522, AW088795, AW194041, AI318244, AI973210, AA027095, T57193, W44853, AA693819, AA860686, N30057, AA825328, AI889552, AI913873, AW050479, AA005320, AA737576, AA010720, AW572031, AV740811, AA843163, AA782544, AI026970, AA772466, AA450017, N71006, AW590986, W32273, AW152339, AI804555, BE169187, AA001714, W32000, AA993329, AA347504, AI263677, AW591684, R91853, AI824356, AI470261, BF431703, AA386154, AA772584, AA632359, AA863458, AA860713, BF574018, AA004243, N94949, AW132079, W32023, AW513318, AI191171, T57088, AW151046, AI289935, AI678407, AI800349, T55946, W05488, R92692, AV744992, C75173, AW512959, BF358693, BE939009, HI3885, D62503, N30060, AI623948, H22323, AW473204, AI344807, AI564394, BF889143, AA450366, T97372, AV741769,

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HEEBK29	835	105645 4	1 - 4861	15 - 4875		<p>             BE745399, AL522262, BE908201, BE906253, AU125614, AW089583, BE621787, AW243446, AV690793, AW192502, A1858615, A1890773, A1970297, AW080065, BE621228, BF475568, A1814791, BE621889, AW960683, AW439633, AU127824, BE046311, A1963657, BF114979, AW090100, AW513648, A1262027, AV696242, AW341634, BE973619, A1963327, A1433025, AW302356, BE620975, AU149236, AW070352, A1806420, AV727879, A1891026, W67512, AA548361, A1185836, BF880354, AW771451, A1815002, AV727886, AW007829, BE677332, A1123019, AA909672, AW514323, AW172713, AW604822, AA565581, A1741211, AW264387, AW380912, AA156812, A1951055, A1884448, AW243679, A1138743, A1922781, AA676839, BE389394, AA317453, BE075417, A1744347, AA063600, BF941222, A1278214, AA780893, BE392908, A1138737, A1372874, AA826478, BF476022, AW088824, AA428436, A1433274, AW074533, H66739, A1348515, BF594677, BE908514, A1087015, AA493387, A1302133, AA742411, A1610422, AV698069, AW303594, AA036681, A1679072, A1985287, A1676253, A1156716, AA983385, AA099281, A1382076, A1204685, AW517675, A1299065, AW515199, W68125, AA443895, N65966, A1628488, A1138741, A1445997, H66738, AW193226, A1499793, A1129495, H43558, AA429214, H42969, AW192218, AV689623, AV691878, A1589031, AV660284, A1888422, A1873783, AA746039, A1985285, A1434459, N95436, AV688537, AA738493, H92124, AW268393, W03866, AA913077, A1537365, A1273983, A1249320, BF312684, H42899, BE466338, A1809446, AA099280, W01930, A1633945, AW771119, N55529, A1129773, W24048, W73426, A1288122, BE906823, W73381, AA826526, AA969783, R94455, A1129884, T03693, A1245885, AA961183, A1866118, N46259, N73753, AA910025, H43559, N81029, AA846611, A1217549, AW515007, AL047369, A1382852, R66548, A1610829, AA927406, F12821, A1625372, AW339822, AA449955, H27222, AA193615, AA88180, H08667, A1372912, A1928559, A1915591, T57021, BF943560, A1634405, AA009986, A1223972, AW513899, T72813, N80311, A1241051, BF061815, AW075328, AV685591, R66549, AW136127, BE166191, AV693190, BF530633, H47698, AA295509, R94163, N94227, AA444089, AV697388, AA380196, BF436805, AA478750, AA582325, AL040492, N71032, BF057259, AW137045, BE965435, A1872536, H08668, H28576, W81416, BF568352, AA699883, F02853, A1926224, A1964083,           </p>

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HCHMM19	836	105661 7	1 - 1725	15 - 1739	AL534327, AI096506, BE378797, BE392697, BE388530, BE563058, AW965878, BE392233, BE392568, BE562786, BE816336, AW602150, BE816332, BF724233, BG012790, AW950293, AW088625, AI623455, BE259257, BE816333, BE712877, BE712851, BE712863, BE712874, BE712876, AW445054, BE392522, BF339456, BE869413, BF353807, BE730799, BE712859, AI378021, BE712921, BE712852, BE712926, BE712924, BE562748, AW089470, BE712978, BE712856, BE712865, BE712923, BE712992, BE712869, BE712985, R54862, BE712979, BE712983, BE713014, BF877112, AI334787, BE712858, BE712997, AW089731, BE712969, AW148926, BE712993, AI565144, AW102888, BE712896, BE713017, BF829674, AA477654, AA410250, R53118, BE764760, BE392951, AW058228, R52267, BE712973, AI688979, AI744763, NS9116, AI061201, R73552, AA410601, AW072414, R54001, H24954, AW243859, AA479843, T53386, BE693883, BF792651, BE712906, AA402649, AI653791, AI499132, AI886419, AA359265, BE712928, BE712931, R48059, BE712934, BE712927, AI887407, AI830659, BE712940, BE713027, BG010635, BE712909, BE764724, R48045, BE712950, BG164045, AA402646, BE712952, AW770834, BE713018, BE713010, BE713009, BE713013, AA411137, BE712949, AI653885, BE712913, BF873070, BE713011, AA358698, AI873571, AA633384, R52266, AI174895, BE713028, AA322308, BE713024, BE713016, BF761627, BF873089, BE713022, BE713026, AA291585, BE712958, AI804837, AI432124, AA394269, BF876486, AL534328, BE713030, AI524776, AA358907, BF876484, BF829815, AA293640, AA430383, R47936, AW193891, AA410602, AW473257, AA411455, AA427751, T53385, AI537722, AA236709, AW028475, BF875028, AA477340, AA427752, AI288000, R06662, AA411583, AA406031, AI860014, AA479650, BE139492, BF353825, AA479720, R35771, AW130914, AA430736, AI684263, AA479554, BF931748, AA428857, R63600, AI870177, AW103389, AW194324, BE712932, C05050, AI538811, AI887289, AA481946, AW150649, BF749660, AI914715, Z19749, AA476975, BE869834, R54871, AI918638, AI684209, BE613048, AA757345, AI525964, AW150617, AA430560, AA402931, AW338545, AI283299, BF740522, AA426533, AA290786, AW438957, AW793096, AA292401, AW439076, BE076592, AA367777, BF036210, AW793132, T47453, AI538248, AI524589, R72922, AI689706, AW450212, AI241778, AW302585, AI683101, AW275299, AA284900, AA989478, BF745978, AW381828, AI873903, R47950, AI918551, AI873999, AA890124, BF445784, AI591415, AI364586, AW593602, AA428332, AA433977, AW089004, AI524580, BE699717,

HE8NG02	837	105662 5	1 - 1215	15 - 1229	AA404739, BF851920, AI648604, AW303547, BE150661, BF825743, BF834926, X83425, X80026, AF270512, AF221507, AB035511, AF246667, A75386, T51317, and AA292790, AI123839, BF439260, T12179, BF679243, AI039039, AI146280, AA236166, AW962409, AA297231, AI147044, AA453695, T12180, AF191770, AF191769, AF191768, and AL035608.
HWHKD22	838	105665 4	1 - 1310	15 - 1324	AI282903, AI986119, AI633646, AI769747, AI984540, BG055419, AW518841, AW337994, BG259048, AI769807, AW518894, AI610118, AW566008, BE674641, AI354761, AI696473, AI150348, AI371756, AW014492, AI815233, AA203505, AA442702, AA811626, AA418029, AV747886, BF884881, BF969470, AV747168, AA808125, AW589703, AI680927, AI632886, AA418089, N70046, AI825035, AW302373, N25678, H39858, AI298620, AI915190, AW770054, R86213, BG149822, N64316, AA810844, AA846497, H28050, AI916429, AI299340, AA633452, BG054552, AW518887, BF447929, AA496038, AL536729, BF446446, AW771301, BF857012, N55216, BF857010, and AK022876.
HOC PJ87	839	105666 6	1 - 1484	15 - 1498	AL518904, AL518905, BE616371, AI828880, BE615355, BE531320, AL513808, BE616160, BE531166, AL530739, AI436189, AI829057, AU119325, BG252803, BF002498, AI192809, AA836407, AU116821, AW006012, BE543906, AA477822, AW170329, AA580307, W74534, AL041460, AI333563, AI589612, AA569804, BE857996, BE780663, AI126528, AI718912, AA428893, AA507376, AA424547, AA769260, AI291503, AW974150, AA410533, BE925853, AA478220, AA022829, W79545, H28373, W84807, AI149621, AA284250, AA410308, BF845479, AA424635, AV749126, AA838115, AI126137, W79363, AW801410, AI221412, AA934373, W01406, AI923931, AA729488, AW613142, BG167622, AW518106, AI357146, W84808, BF737247, AA253039, N70789, H25595, AW801537, N68230, AA022828, BE812559, AW801332, AA352675, AW176646, AW401979, AI749443, AA292613, AI985391, N36778, H28398, T29515, F08556, N45939, N77827, AA193262, H25550, AW751653, AA937981, N28457, AW081522, BE000431, AA814116, BF748285, BF760942, BE183148, AI188907, BF056502, T25961, AW366647, AI340862, AV686817, AV689385, BF986723, N87297, M25393, S52655, M80739, M81477, X58828, and M81478.
HAAAA59	840	105667 1	1 - 6052	15 - 6066	BE890597, BG109730, BE733024, AU140104, BE889571, BE546473, BE889587, BE730721, AU138672, BG259764, AI718282, AI709383, BG163913, BE779177, BE734224, BG031798, AV707879, BE408475, AW368622, AW272235, BE900705, AV721483, AW470101, AW471310, BE891068, BF435568, BE386130, BE901385, BF980199, AW392816, BE894916, BE220160, BE903247, AW392815, AW076072, AW392813, BE734460, AI671707, AI628226, AW572916, BE540311, BG122367, BE273197, AW499944, AW769234, BG235985, BE549113, AW470123, AI138202, AW629754, AI887486, AI984572, AW996987, BE296360, AL353974, AA732450, BF895267, AI859535, AW080807, AI523527, AI752689, AI693382, BE892451, AI984050, AW131290, BE048752, AI922765, AA777248, AI832002, BF185637, BE048701, AI346505, AA922780, AA521201, AI954924, BF844854, AU157701, AA557382, AI888131, AW269811, AI608617, W72219, BF698993, AI681187, BE559573, AA932106,



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HOSBJ18	841	105667 2	1 - 2689	15 - 2703	AUI32197, AUI35985, AUI38727, BG260506, AV726837, BF793520, BF345717, AV702929, AW439565, AI827530, AI887525, AW118200, AW801248, AI890158, AI859703, AA167094, BE175387, AA430563, AA883993, AA029288, AW662754, AUI57723, AI095763, AW630944, AI279436, AW937419, AI634574, AA749212, AW966597, AI598263, AA993239, AW662852, AI079917, AW243702, AI634584, R70961, AA971019, AW780141, AI926025, AA043743, AA452390, AW131171, AI219729, AI610785, AA969116, AA132531, AI818902, AI243449, H02869, AI922025, AUI58190, AW627656, AUI55589, AA021150, AA433979, AW769987, AA579993, BE165647, AI220990, AI469540, AI300047, AA621433, AA029756, AUI31744, AV755425, N51151, AA166907, AUI56407, N47896, AI288925, AA888601, AA912768, BF674302, AV708374, BE175399, BE832329, AUI26967, AI926028, AI183313, AA937998, AA602187, BE734288, BE706930, AA834867, BE251990, H03766, BG027418, AA132592, BE253942, AA866089, AUI56259, BE255873, BE256052, BE257877, BF348897, BE254914, AV705050, BE255702, BE536889, AA342184, AI873839, BE257993, BE161730, BE251753, AI017196, BE256952, BE254487, BE886141, H88995, BF915387, AW749734, AW887332, AW367251, AA369249, AI926057, AUI23294, BE927508, BE880918, BE673902, BF335051, R68839, R70915, AW367256, BE901334, F04001, AW250092, AA911119, AW386242, AA336851, AW367300, AV764447, AW384427, AA043742, AA028917, BE900678, BE843977, BE767608, BE938819, W52994, AA349969, BF351610, F07748,

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HPDRG02	843	105676 4	1 - 2158	15 - 2172	<p>AJ238010, AJ276253, AJ276255, AJ276256, AR096545, AR064707, DI7247, A93923, AJ276254, A93931, AJ276257, A93916, A85203, AJ276251, AL133053, AL122101, AL133082, AL133074, AL133049, AR023813, and AL133019.</p> <p>BE740652, AI823584, BG171310, BE878882, AW411439, BG166780, BE906086, AI738670, AI815554, AW411440, AI056402, BE262512, BE877434, BE537553, BE789460, BE867534, AI658796, BF035412, BE875754, AI634741, BE617343, AW393490, BE876210, BE871919, BF340756, BG024047, AW820946, AW373531, AW820897, BE048051, BE879337, BE048598, AI819079, AW571769, AW364602, AW580228, AI968762, AW245315, BF590952, AI674100, BE071871, AW580233, BE876307, AI869292, AW384848, BE620263, AW152279, AI262789, AW820801, AW608412, AW731673, AL529564, AW574850, BE271554, AA209480, AI755183, AI589643, AI656369, BF338937, BF475268, BE934850, AW401380, AV700085, AW236549, BG231513, AI687271, AU160081, AA847360, AI418295, AI985588, AW119103, AI217351, BE909190, AW016080, AW608420, AW131023, AA630269, BE464492, AI149427, N78179, AI459620, BF593096, BE879192, AI554812, AI640839, AI289506, AI268192, BE313248, AW513453, AA931552, AW058369, AA813634, AI347031, AI804259, AW090211, AI023516, AW069813, AI752976, AW820999, BG116353, AI088760, BE502154, AW402830, AA768964, AW002017, AI075703, AW673691, BF912726, AW613623, AA501894, BF056551, AI869699, AW117841, AI879509, AI587532, AW088852, AA419154, AI860748, AW590575, AW820882, N23571, AI083954, AA551989, N36125, AW118704, AI582641, AA430497, AI014467, AI159184, AI969972, AI263126, AW276084, AA707165, AI469114, N22868, AI816495, AA858117, AI857776, AI018617, AI086473, BF993501, AW975321, AA430615, AW771778, AW860492, BE940584, BF912687, AW821020, AI499659, AA577158, AA134113, BE146324, AA226941, N26266, R52309, AA035350, AW022630, AI628121, AA411681, AA974019, AW664863, AW072821, AI992296, BF813511, BF594364, AI880357, AA846048, BE933452, AI564340, BG168373, BE873734, AW072810, BF806150, AW276091, BF951215, BE873926, AA503631, AI695958, AA135227, BE878360, AA159279, AI357749, AI688770, BE076556, AW997254, AV749793, AA113061, BE784393, AI559423, AA884640, AI332794, BE935220, H79618, BF949317, BF949336, AW406267, AI984860, AA337025, AW378543, AA302570, N59626, BF087435, AW025306, AW821028, AV683126, AV688200, AV691923, AI203166, AI632661, N93344, AI424079, AV696315, AA330793, BF756713, AA079425, AA280167, BF816528, N33283, AI066652, AA603468, H56757, AV684426, T90349, AA227048, BE463449, AV697361, AW378523, BF886853, AW449882, W78180, AI203210, AW663171, AI886503, R37349, AA336361, AV697357, BE149771, F12979, AW378539, BG164953, AA291431, AW820943, AA515270, AA636029, BE900663, AA227036, H98849, AA113144, AA216614, AI270424, J05016, J05186, M86870, Y00884, T93550, T75358, T88819, T83030, T84206, R12463, R15281, R38684, R54472, H56677, H61562, H79619, H85766, N33287, N44131, N73592,</p>
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HHAWB19	845	105677 4	1 - 2149	15 - 2163		BG252201, AV726464, AL529709, BE894106, AV726994, BF970560, BF132059, BF977798, AI703275, AW512938, BG164577, AL529708, AI767521, AI823746, BE220262, AA583438,

HHATP38	846	105678 6	1 - 1140	15 - 1154	<p>AI143608, AW468337, AI949854, AV727138, AI620344, AI209187, AI630993, BG007081, AI004986, AI565892, AV715169, AI367983, BF056815, AW394003, R70620, BG007658, AA152183, BF381743, AA565300, AA088574, AA931697, AA995899, AI025252, AA297479, T84083, AW138535, H71679, Z45535, AA297478, AI865989, AA367654, AA150060, AA044326, AW338484, D29436, R24591, AI005551, H00983, H39751, AI669105, T83438, BF091777, AW138127, R21165, BF083909, BE934286, R76620, AA971307, AA745052, AW945769, AI554153, T84151, BE550213, H01724, AW051517, AW373316, AW373313, T99390, BF083903, BE541509, AA180271, AI263504, AF140242, AI133390, AF140241, A68713, and AX013137.</p> <p>AL529876, BG167387, AI300509, BF034876, BG031449, BG164001, AI471460, AI524696, BF314865, AA633535, AW242169, AI141331, BE045747, BE221399, AI805778, BE297480, AA843665, AI571521, AI299824, AA434485, AA434389, AI569021, AA843530, AA082818, AA741539, AI805251, AV704867, AI308147, BF128614, AI091655, AI308088, BE904001, AI749633, AA746258, AA040199, AI497961, AA948212, AA040843, BF197824, AA742966, AA983317, AI371855, BE783995, AW952041, AI420031, AA469054, R56770, AA535588, AA352350, BF850175, AA292448, AI284332, BG167521, AA630120, AA400486, AA310070, AA182397, D80973, AA304346, AW770337, AW606565, BF876874, R88630, H28025, H39505, D80974, BF054728, N87395, BF054746, AA932606, AI581555, R90829, AA400532, AI720121, F32140, BF197523, R90830, AI687256, BF876828, BE157170, BE157094, BE157173, BE157093, R29477, T08411, BE157099, BF751287, BE157098, AA419103, BE157092, AA917955, AB004273, U43368, AB004274, U52819, U43836, AR060515, U43369, U48800, U52820, AR060517, U43837, AR060512, AR060513, AR060511, AR060516, AF022952, AR060514, AF032925, AF099134, U43370, and U80601.</p>
HVVBE07	847	105680 1	1 - 1125	15 - 1139	<p>BF115907, AI347987, AW571531, AW469391, AI318417, AW469530, BF732916, AW519112, AI745619, AI624640, AI148123, BF439103, AW246565, AI049532, AI141077, AW304970, BE328487, AA417098, AA838314, AA649876, AI954020, AI347379, AA614714, AU155615, AA029774, BG057767, BE350234, AI241721, AI422257, AI148124, AV721594, AI359911, N70830, AI359059, AA159067, BF968305, N67615, AI049846, AW015705, AA009674, AA373582, AI174368, T27684, T56814, AA069201, AI267963, AW118346, W73079, H81485, AA121951, AA055076, W07306, AI191548, AI808436, R40817, AA035256, AA773059, AW166460, AA773057, AI214117, N93955, AA156330, AW675349, AA872378, BE793803, BF982619, BF858206, BF858207, T29598, AW956178, AI252634, AA629421, AA055136, T56813, AA302186, H25812, AA308949, AA418136, BF208253, AW023605, AI611964, AA977778, AL524944, T50650, AW166214, AL037765, AI741822, BG036833, BF953193, AI916187, AW899528, BF207696, BE881367, AA081611, T47416, AA393875, AW496811, AL036550, BF822724, AW082037, AK025842, U60477, M64497, I89201, X76653, U07635, AF003944, AJ249441, U00697, X16155, X12795, M62760, AB012582, U16683, U50354,</p>

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HKAHB85	848	105680 4	1 - 1339	15 - 1353	AI189624, BE798410, AI826306, AI742365, AI923164, BE742614, AI523767, BE612598, BE730876, BF568739, AI743357, AI923662, AI874405, AI582377, AI951036, AI830906, AV722920, BE857117, AI864666, BE552477, AW269479, AI453638, AI658863, AI609762, AI935343, AI762473, BE251544, BE966347, BF059081, BE222650, BF434095, AI457104, AI192517, AI262763, AI312553, AI128385, BE392107, AI184898, AI208329, BE780463, BF111625, AI937815, AA156715, BE613338, AI084901, AI923949, AA156811, AW007906, AA478088, AA516138, AW194068, BF593875, AI074507, BF590787, BG054965, AI123728, AI923959, AI342586, AA725089, AI199610, AI369183, AA039529, BF000406, AW500544, AI694026, AI743576, AI285358, AW298302, BF242393, AI559628, AW803113, AV724161, AI472176, BF941760, AA135658, AV724606, AA714301, BF115666, AI830771, AW512691, AA846737, BG248683, AW006013, BE796082, BE889162, AA559059, AA887841, AA742700, AI910998, W45621, AA514670, AA047549, AA039510, H12597, BF221654, AI675498, AA075686, AW136156, AW628392, R36089, AA188215, AA340528, BE674700, H12647, T28463, BE219841, W28363, T19366, T19367, AA186362, AW044216, AA872728, BE796300, AI869260, AA419332, AA079138, BF130394, H26663, AI864116, BF182762, AI908177, AA328427, AA287370, AA425996, AI022515, AI015637, AA018470, AI935563, H30032, BF309963, T39530, H26648, AA283917, AI201855, AA018144, AW002235, AA147931, AI970783, AA074201, AA453079, AW967024, AA666180, AI767839, AI818846, AA971961, AA522463, AA971644, AI908203, W45569, BE267358, H20096, AI658744, AA524207, AA147502, AI560299, H20021, H23586, AI695631, AW028597, H19534, BF213007, AA057785, AI695962, W15192, BE392656, H30033, AI864118, AA047837, AA283918, BF315308, AA452911, T64430, AI935201, AA477630, AI911950, AW663032, BE264884, AA810162, BF183741, AA514790, AA425791, AA706619, BE378391, AI249587, AA135599, BE817810, AA399044, AI792444, BE872189, N78686, AI054233, AI053971, AA018145, AI191224, BE049111, AI523309, X12794, AF003926, X76654, L25674, and AW002470.
HUSXA15	849	105681 0	1 - 290	15 - 304	AL524678, AL525517, BF968916, AI954468, AI567133, AW300897, AI669011, AI660855, BF448589, AI635690, BG236776, AI815794, AW874612, AI480193, AI366904, AI537283, AW593618, AI817467, AI751715, AI366942, AW593632, AA459301, BE047378, AI016670, AA477441, AW161913, AW161619, AI926577, AI859809, AI983583, AW001554, AW264376, AA284935, AA404681, AW088937, AI038308, AW440417, AA653631, AW262712, BF115584, AA058887, AI984462, AW249502, AI798533, AW172776, AI750245, BG056549, BG055715, AW131904, AI864472, BG223340, AI434101, AI219769, AI028334, AI476359,

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HOCPP16	851	105685 6	1 - 1027	15 - 1041	AL522455, AL528025, AL532452, AL523902, AL524678, AL528052, BF340685, AL525320, AI815794, BF526000, AI800143, AL527163, BF337577, BF116185, AI926577, BF206655, AL530392, BE383255, BF206587, AI480193, AI499226, BF207314, AI669011, BG257349,

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HNOAH83	852	105686 2	1 - 1537	15 - 1551	AL529607, AL525913, AL536158, AL520415, AL520414, AL526120, AL529606, BE871581, BE799282, AU119186, BF337601, BE908277, AA826247, BF344321, BE273446, BE797849, AI127898, BG115251, AI809875, BE880755, BG169799, BF525762, BF526032, BE907671, BE872651, BE407091, BG119008, BE908601, AL529168, AL529167, BE910353, BE868097, BE548520, BE617451, BE250135, AV707005, BE870326, BE898755, BG251022, BE311912,

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HODGM46	854	105692 7	1 - 870	15 - 884	AW963219, BF924687, AW407007, AI125143, Z36862, BF817511, AA847341, AL044966, AA837771, AA582746, AA557945, AA610255, AA368329, AI732911, AA579082, F35684, AA522864, AI459879, BE049455, R67701, BF934303, AV732057, AA635150, AU147226, F26395, AW021674, AI633386, AI559720, AW028376, AV730440, BF950367, AI468993, F00937, AA745302, AA846046, AA640563, AV760155, AI251024, AW237903, AW089395, AW471494, AA354868, AA158549, AI915081, AI370470, AI445699, AI538404, AW275432, BE156328, AV714079, AF236698, AI444575, AA507990, AI519329, AA219166, AI308529, H47461, W69639, BE409402, AA610644, AA825954, BF724945, AW407679, AV649510, AA015948, BG059924, AI367551, BF815277, W45215, AI572680, AA351868, AA506734, AA368659, AI636734, BF914861, AA507291, AA569206, AI246386, AW979184, BF965924, BE207536, AW238016, R79396, AA935827, AA578245, BF772886, AL135490, AW196288, AI520984, AI828721, BE889093, AW029626, BE149998, AA661590, BG178582, W45416, AA460786, AI355246, AA155817, H29914, H68343, AI888050, AI921765, H79277,

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HODFR44	855	105699 0	1 - 728	15 - 742		AA897542, AI918140, BF975472, AI015702, AA586867, AI086135, AI858527, BF306114, BE300941, BE298569, AI090918, AI191755, BE328004, R59186, BF204020, AL524762, AW075596, AA291767, H07084, BF827044, BF737073, AA291766, H53735, AW206845, BF690570, BE019345, BF305732, AA909455, BE397797, AA921923, AI290282, AW954906, R38009, AI479903, T27152, BG222851, H53734, AW361311, AW627470, BF737063, BF761437, AL137516, AK025712, and AC022515.
HCHND12	856	105700 9	1 - 391	15 - 405		BF155196, BF151195, BG222449, AW371240, BF990033, W07572, BG013608, BF736389, AI907180, BF759690, BF742354, BF350339, AI671621, AW236992, AW410534, BF108852, AW057736, BF743441, BE297998, AI906106, AU140362, BF743462, AI907178, AI907188, BF984645, BF083392, AW371253, BF083378, BE155590, BE858290, BE698057, BF084125, BE091682, BF083386, AR034479, AR080259, I21124, AB008451, I21129, D16295, AR082744, AX023363, U71126, M11765, M12036, M11764, and AR086088.
HBHAC29	857	105715 7	1 - 802	15 - 816		BF944637, R17484, F11360, BF364648, BF957813, BF967711, BF090330, M29273, AC002132, M22357, M31811, I07878, J00756, M36702, I00254, M14871, X05301, M16800, X06554, M74787, and X98405.
HTPFW87	858	105717 0	1 - 2298	15 - 2312		AI889084, AW583210, AW583210, AW583686, AW583840, AW582954, BF883469, C06313, BE045909, BE045774, BE047051, BE045791, BF913619, BE045879, AW584003, BE042657, AW583474, AW862527, AI274789, BE045869, AW583430, BF197864, BE045900, AW087963, C06104, AW583020, AW583372, AW371544, AW582943, AW873924, BE045778, AW583323, AW873944, C05994, BE045797, AW874333, AW293311, AW873851, AW873852, AA845062, BE045910, AA845140, AA844754, AW873837, AA921397, AW014253, AI249954, AW583254, AA804606, AW873893, BE047058, AW874447, AW873952, AA405888, AW873926, AW338510, AI566621, AW874339, AW873937, BF755849, AW873888, AW242204, AW873810, AA835252, AA844759, AA405728, BE970129, C75365, T11187, AA845117, BE969807, AA845035, BE969825, AR012827, M54994, AR048597, A31800, M85201, S79774, AR012828, AF081673, M28402, AR022356, I41327, X16054, M15893, Z22803, AF072711, I38891, M94579, AF206618, X65944, AC002097, I14813, AC000395, M94580, AF206619, M69157, S70516, S70517, S40178, U52425, AC000394, and AR012831.
HISAF60	859	105721 2	1 - 3598	15 - 3612		AL524621, AL521404, AL524622, AL521403, AW978618, AL529722, BG256352, BE909801, BE783472, AW953057, W60630, W29012, AA149513, BF968833, BE783711, AA149644, AW965598, AW977554, BE834598, AA306190, AA404374, AA928795, AW026671, AA733045, AI131505, AW051295, AI139050, AI144018, BE855656, AW162934, AI089282, AI571763, AI351676, W60631, W76344, AW005213, AA146937, BF366791, AI146486, AW262622, AI557215, AA635131, AA780109, BF734995, W74364, AA978196, AA029134,

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HRABO80	860	105721 9	1 - 2303	15 - 2317	N73970, BF477084, A1755166, BF061416, AI920880, AI925857, AW072087, BE044048, BF754597, A1215589, A1354891, AA659919, A1271925, A1635236, A1248143, AA419156, R74346, AA419119, AA477132, AA326493, AA904372, AA477379, R74443, A1187966, BF941777, T33009, N91382, R72137, BF928844, Z45408, Z41119, AA666033, AA385063, BF448827, AA349368, BF196368, AW953123, BF941802, BF940219, R72086, A1932928, BF849745, BE707723, AA091149, BF090935, A1040362, A1264069, AA464975, A1346211, R55970, N99981, AA133535, A1276142, BE466055, W79505, AW206373, AA115760, R08200, A1679070, A1934793, BE936729, H44191, BE936715, A1953019, R55612, A1677914, T87783, AA465043, AC005237, AL050143, and AK025374.
HADDF30	861	105726 0	1 - 1524	15 - 1538	BF035536, BE466525, BG249577, A1923884, AA181023, A1420093, AA234461, A1580216, A1818510, AA186658, A1079954, AW150282, AA236533, AW851143, AA056421, AA132695, A1823407, BF768062, W39381, W38356, N79807, A1537664, AA913663, A1808322, AA913197, A1758115, AW974105, AA569156, AW609148, BF852368, AW605579, AW609171, R01697, BF852380, BF242772, BG033123, A1473441, R68282, AK025934, X54989, S69002, M21829, AJ001482, and S82592.
HDAAS58	862	105727 2	1 - 737	15 - 751	AL519465, AL529166, AA016096, AW499988, A1936646, A1905303, BF794653, AF254082, AF254083, AF254084, AF254085, AC005003, AF119256, AF242522, AL096880, and AB029397.

HSDZG15	863	105730	1 - 1279	15 - 1293	
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HHESW02	865	105747 8	1 - 1876	15 - 1890	AA551061, BG034640, BF001802, BF795036, AV764202, BG032289, BG259953, BF979110, BE408962, BE561363, AV760691, BG033633, BE348456, BF854361, AW402086, BF062592, BF691935, W46419, A1952866, A1718495, BF691364, AA970444, A1289901, A1095214, A1061277, A1347580, A1826942, AW511617, AA312289, BF217041, AA484029, BE560239, N68961, BF088217, W49781, BE246728, AA962522, W00660, W48762, BE729436, AA577013, AA354415, AA328452, AA989644, C01310, A1970883, AW513997, BF810694, AA355219, AW955293, AA361050, AA327850, A1264968, AA360699, BE246766, BE826080, A1087069, AW058063, AW856095, AA829953, AA358539, AA337078, BF433442, A1525090, AA319325, AW869241, AA381176, A1905583, BE711695, AU076504, A1688129, BE832438, AV651700, AV707405, AW955686, AV727550, AV709358, AF062075, AF118146, X77598, AR086332, and U38894.

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HEOADI2	869	105784 2	1 - 1124	15 - 1138	BF307050, BE294659, BE295378, BE270183, BF306043, BF304968, BE299101, AA380349, W19499, BE832758, AW882273, AW263540, AA157229, AA225180, AW409843, AA151564, AA909334, AY009951, and AF116865.
HVVBT41	870	105788 0	1 - 1835	15 - 1849	AL520942, AL520941, AL524223, BF975546, BE790646, BE250104, BE741659, BE908458, BF346226, BG253282, AI992170, BE271697, BE891409, BG116444, BG032571, BE383072, AL534026, BE390699, BE257602, AL534027, AL134371, BE250877, BE790095, AA527588, BF316156, AI249023, BG170667, AL524222, BF313879, BE393833, AW007167, AI193019, AI435295, AW249684, AA315000, AI887652, AW160553, AW629814, BE831627, AA419118, AI878843, AI143093, BE795572, AG39468, AI762318, AI141843, BE305036, AW630286, AI093040, BE272301, AI355887, AI469829, BG059403, AW058047, BE891650, BF432375, AA769826, AA516117, AW954502, AW406598, AW245217, AI500434, BE907766, AI360848,

	871	105791 5	1 - 877	15 - 891	<p>AI360627, AA829263, BF973383, AW162348, AA292739, AW305301, AF150177, AA829261, AI026015, AA065261, AA468594, AI570428, AI272753, AI025635, AI431477, AI356413, AI285290, AA723167, AA772406, AI758572, AA419155, BF896723, AI567444, W60078, AA292740, AA426124, AA804359, BF901807, M78872, AI879402, BF817528, BF924799, W27536, AI093981, AA456338, AA065263, AI050976, AL536719, W52850, AA065262, AI499057, AA494517, AI202110, AI191772, AA393388, BF882870, AI969483, AW613776, BF093157, T50063, BF857386, C18340, AW515520, BG115358, BF093166, AI933649, AI361629, T12239, BF899941, R44560, AW058070, AI360335, N31024, D63172, BE645919, AI621352, AW889390, AA454691, W69640, AW467694, AA378222, BF752025, BE174966, BF343963, AI249913, R24856, AI564653, AI653909, BF992556, R46328, AA478329, BF528267, W67832, AA410700, BE546949, W67968, AA233391, BF768160, T69638, BF093158, BF093167, AI567607, BE939001, T35071, BG249527, BF834920, BE378906, C00258, BF090917, BF760706, AI985993, BF804516, BF948632, AW867372, AW379505, T10814, AW799935, BF829924, BF753005, AA446743, BF951549, BE305164, AW867554, AI874375, AI902997, BF821220, H44663, H44749, BE293464, AW961410, AW958927, AL035587, U80744, AF161347, AR018138, and AI499044.</p> <p>BE618433, BE264353, BE313324, BE263795, BE383317, AI912683, BE618668, AA779820, AA991941, BF337731, BF965805, BG149406, BF057515, BE550120, BE793000, AI161191, N92707, AA926829, AA602406, AA911645, AI032667, BE503970, AA844970, AA576535, AA936479, AI094810, AI312822, AI365506, BE264410, AI143188, AA677341, AI091456, AI298331, AI273560, AI094902, AW470381, AI095731, AI277885, W79024, AI161190, AA729304, AI393476, AW949867, AU126753, AA948313, AI355600, AA861985, AA922331, AW160933, AA719310, AW162238, AI161149, AI041523, AI339212, AI014445, AI078542, AA987978, AI078619, AI350176, BE464539, AA935049, AA972852, AI817990, AI312673, W15310, AI935214, W39738, AI669550, H42852, AI873672, BF508021, BF437071, BE673460, AI873653, AI095798, AA991983, AA115875, AA594838, BE925134, AA534320, AW964391, AI240950, BF748841, AI092670, AA502784, AA580530, AI219314, BG152840, AW162538, AI432612, AI424202, T29324, AW381155, AI972574, BF350356, AW381156, AW381157, AW381154, AW381160, AW381158, AI673210, AA902771, AI865515, AW381367, AA340935, H42452, AI700003, AI141677, BF061619, W20323, AA297723, N84685, AW237917, BF847511, AW371365, AA594920, AW160737, AA364730, AA700832, AI740998, AW381361, AI971961, T19132, BE646310, BF058452, AI873154, BE299714, AA129778, AW381159, AA129681, AA371867, AW518312, N91971, W24300, BF941876, AW189399, BF933605, AA933767, AA628047, AA115874, AA911071, AL119457, AL119324, AL119399, AW877209, AI284131, AL134524, AL042544, AL043152, W95140, AL119443, AA745155, BF213477, AI961590, BF034010, AW804686, AW081670, BG176595, AW392670, M11433, X07437, X60367, M36809, M16459, M19257, X07438, AX030435,</p>
HAZAE42	871	105791 5	1 - 877	15 - 891	



					<p>             AJ251859, AX046357, Y11587, AR060234, A81671, AR083266, AK026480, AR054110, AB026436, AF090900, AL050170, AK027001, AR066494, AF067728, AX042059, AR069079, X53363, X51694, AJ279014, AR055519, AJ012288, AF007142, A17115, A18079, AR038854, AF026816, AK027081, S36676, AF130099, AF076633, AC010202, AF199027, AL137533, I77092, E13998, AF131821, AL117416, AB040710, X79568, AL080148, AL333625, AL080154, AB048954, AL133016, AC003001, AK027144, AX040958, AL137716, AF130056, and AF060866.           </p>
HPREN60	872	105794 8	1 - 1292	15 - 1306	<p>             BF337618, BE255115, AW603700, BE896817, AW603677, BE672938, BE276149, BF574363, AW937845, BE252116, AW849081, BE561148, AW376536, AW849079, BE514132, AW384020, AW384003, AA043138, BF348905, BE560153, AL047014, AA152015, BE156263, AA147575, AW384016, AW848806, AA594982, A1825953, AW937773, AA446384, BE396902, A1422448, AW952134, A1160548, BE856434, AA211287, C03422, BE385571, AW384004, AW381024, A1572008, BE730503, H10239, F36732, AAS28114, BE706949, BE156337, AA152022, Z33590, Z37011, AA040869, A1149862, N49013, BE156286, R84898, F12229, AA152219, R56182, R54122, H26826, R55910, Z24984, H13040, AW875889, AA318749, BF994321, Z25108, R13067, BE857659, BF477403, H26349, T66390, BF673084, BG010755, H22780, AA030050, C04576, AW516130, BF692959, F26947, AA429964, D57868, R20192, F29092, BE858947, F30389, D62688, C16326, A1096674, F09858, A1139180, A1201475, AW390825, Z28845, AA443358, A1139454, AW068999, R40498, AA037606, A1373942, T25134, AA156446, C16141, D57713, AA152096, F18878, A1032649, AA090702, W59970, Z28703, AW190966, A1720482, R56071, A1339673, R55825, A1368681, AA595134, C16104, BE706948, BF350778, AA993887, BF445806, A1147605, BE156340, H05938, A1200609, D57624, D57229, AA211332, D58131, D57532, A1582955, A1148481, BF978143, N48284, D56502, AA972352, AX013692, AF002282, AF039018, AF002280, AF002283, AF002281, and AJ249218.           </p>
HOVCZ68	873	105795 8	1 - 2115	15 - 2129	<p>             BG116678, BF243086, AA460133, AV662045, AV687215, AV724260, AV702152, AW450588, BF438173, AA236796, BF214971, A1653152, AA700186, AW963679, BE740138, A1692488, AW885555, A1744585, AW293745, AA693931, BF983866, AW304368, BF195586, A1214602, AA236842, BF360988, AA461488, A1341662, A1653052, AA701860, BE563637, A1420813, A1695758, AW296315, A1864175, AW957517, A1214697, A1022448, A1246345, A1038613, A1638793, A1631642, A1805779, AW019975, AW020821, AW068525, BG179259, BF223132, A1633543, A1655217, AW608280, AV693632, AW886582, AA374097, A1905366, AA450279, AW026664, R00254, A1002466, AA244063, A1391492, AA194965, AW885727, A1249184, A1811272, AW594616, A1420637, T55576, AA340655, T29589, A1168319, AA404500, AA384360, R01927, AA373240, BF360633, AV690607, AW883206, BE833779, AW068788, AV684001, AW367046, BF063831, AW884828, A1271355, R00364, BF588606, R01976, AW605113, AW883935, AA195600, A1263408, AW886854, AW885124, BE833700,           </p>

H6EDF71	874	105797 9	1 - 1188	15 - 1202	AW884903, BF221516, BE833419, AW884834, BE833389, AW884738, BE833749, BE833442, C00050, BF835575, AW885144, BE833470, AA460134, AI014726, BE933542, AW193605, AW772678, BF832527, BE833582, AW055115, AW275486, BG115992, AA723812, BE833498, BE833745, AW886485, AW882507, BE833440, AA024439, C00678, AI802365, AL514359, AB010829, M63123, I09271, L21716, X83377, M19481, Z29532, M36512, M19529, M19480, M31591, X87609, S69801, M31588, M31590, M31589, M31587, and S77841.
HCOOF60	875	105800 1	1 - 1061	15 - 1075	AL520437, AU142804, AL529893, AL532350, BE746380, BE790665, BF338510, BF032858, BE879618, BF685188, BG111720, BF038502, BE876973, BE874884, BE514853, AL520436, AU128255, BE746932, BE271355, BE878839, BF037429, BG260711, BE929847, BE787588, BF085958, BE929836, BE394324, BE514701, BF034098, BE745477, BF032757, AI961479, BF034418, AW190446, AW580763, BF856484, BE929826, BF085962, AW794866, AI923277, BF036383, BE271711, BF367936, BG163405, BF036043, BF085965, AI884400, AW129387, AW470030, BF085961, BF367954, BF838606, BF033708, BF155010, BE929780, BF893428, AI432621, BF112058, AI701980, AA478755, AA418709, BG003366, W93910, AI635480, W93648, BE929849, BF792654, BF094272, AI491762, AA418855, AA918056, BF792592, AI270167, BF874313, AA938271, AA558268, AI707674, AI338213, AW803891, AW178327, AI613026, AA418701, BE880059, AA471190, AA455447, AI082024, AI476785, BF834237, AI280720, AI275229, AW817309, AI708271, AI742309, AA588253, AI167998, AI857345, AA455448, BF315654, BF089052, BF089047, BF831778, AA834685, BE825546, AA669129, AW090377, AI445021, AI016116, AW749412, AW662036, AA773707, AA773711, AI474588, BE094468, R31499, X69398, Z25521, AB012693, Z25524, D87659, and AF017437. AL526177, BE253593, AL532360, BE799956, AL527147, BE798900, BE731866, AL526332, BE791805, BF311672, BE887602, BE887139, BE906158, BG032280, BE274611, BE790863, BE747125, BE793231, BG033981, BE794214, BG105698, BE795680, BE883369, BE314315, BE88057, BG030175, BF037460, BE269400, BE798571, BF794891, BE382478, BE889569, BF205550, AL524393, BG165274, BE612547, BF315624, BG122586, BE262243, BG036814, BF968944, BE729909, BE264533, BE887730, BE252503, BE267719, AI678077, BE728326, BE292738, AI884863, BE407519, BE885803, BF206103, BE278817, BG177708, BE880576, BF317101, BE513876, BE207288, BE793544, BE794750, AI869333, AI884942, BE621419, AL524942, BF689214, BE562063, BE268715, BE907860, AI532359, AI859296, AL524941, BF317484, AA829937, AW250313, BF308280, AW300936, BE782513, AW665495, BE542407, AI571293, BE730436, BF792913, BG179097, BF969617, AW674596, AW273060, BG250687, BF684404, BF205595, BF970179, BG056166, BE312868, BE891748, BF971047, BE261776, BG116513, AW615753, AW248281, BG167242, BF035772, AA582906, BE297066, AW615587, BE392439, BF203659, BF128828, BE896101, BE884376, AA928110, BE781600, BE408171, BE780535, BG122278, BG031477, AA283711, AI589898, BF038700,

					<p>BF304160, AA594105, AA828316, AI038859, AA906924, AA938955, AW170665, AW172642, AW248955, BE882140, BE314300, AA975490, BF984294, AI123879, AI367867, BE269633, BE905299, AI826097, AW070748, BE207170, AW272915, AA316879, AI089508, BE047759, AW732128, AI086474, BE867778, BE270447, BG037185, BE295291, AI566244, BE263223, BE904265, AA661759, AI015067, BG027133, BE737539, AW245061, AW000868, BE905830, BF307405, AW409921, AI538087, BE22076, AA688299, AW250988, BG248928, AA827720, BG109965, BE883149, BG115653, W58033, AI953468, BE908677, AA211097, BE906230, BE965528, AW078745, AA994072, W79220, AI891144, BF793158, BE410412, AL524392, BE622905, BF303849, W74508, BE276424, AW102638, AA918328, AI471577, BE790070, AA826730, AI922589, BE613119, AA991461, AA969243, D56355, H51344, BE044549, H73020, BE908097, BG118308, AW089131, AA355115, AW340401, BE048131, BF688572, AA210923, BE791308, AA290724, A271034, T19021, W57949, AI362888, AI349002, AW075177, AW075033, AW956171, AI307208, AI348921, BE049086, AW073656, AI252463, AI345565, AW072513, AI307493, BE139361, AI255068, AW072520, AW301481, AW075006, AW074809, AI349195, AW074937, AI583896, AI251662, AI610913, T29587, AI246087, AW071374, AI313336, AI269525, AI340589, BE139280, AI334733, AI250128, BE301331, AW072901, BE138965, AC005324, M91670, AJ388535, AB011473, AA876186, AI053722, AI054057, AI054060, AI054079, AI054172, AI054217, AI054302, AI054335, AA496649, M91218, AI247038, AI251232, AI251262, AI251264, AI251289, AI252075, AI252160, AI252427, AI252839, AI252868, AI252926, AI254494, AI254764, AI270156, AI270787, AI271496, AI289711, AI305762, AI307442, AI307473, AI307478, AI307559, AI312145, AI334881, AI334886, AI334909, AI340619, AI340643, AI340734, AI345036, AI354978, AI865061, AI802837, AI802853, AI802854, AW071289, AW071307, AW071311, AW071420, AW072496, AW073049, AW073433, AW073456, AW073469, AW075100, AW075181, AW271039, AW271867, AW301901, AW302085, AW302327, AW302733, AW302738, AW304648, and AW470478.</p>
HVV/BH81	876	105805 9	1 - 3719	15 - 3733	<p>AL518676, AL518677, AL531304, AU141086, AU118214, AI373164, AU133052, BE270816, AU135714, AU120690, AL534584, AW850569, BG116153, BF980876, AU131160, AU124508, AU126480, AL042922, AL531305, BG257200, BE882992, AU133074, AU136504, AV728061, AV726133, BG258667, BG181161, BE893908, BG252256, BF983502, AV757242, BG260910, BE891169, AI831087, BF983539, BG250922, AU139474, BG251940, BE542434, BG250000, BG027005, AU127917, BG032069, BE897086, AU130237, BE891054, BE897202, AW105385, AU127922, BE087523, BF795690, BF797994, BE294893, BE514490, AV712214, BF791761, BG108276, BE888881, AU123253, BF672104, BE904546, AU122800, BE268292, AW991449, BE874925, BG114816, AU120326, AV715180, BE886051, BF982166, BE879865, BE304478, AW604316, BE268335, AW377087, BF681298, BF304610, BF690679, BE620261, AW953561, BE871794, BE514422, BF696991, BG120797, BF686663, BE784110, BF245659,</p>

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HSPTJ51	877	105817 2	1 - 3338	15 - 3352	<p>AA773287, AA993499, AI032485, T24851, T16570, D29179, F12684, F13659, F10295, AI252212, AI262257, AI273428, AI307318, AI367963, AI371950, AI380309, AI446149, AI494183, AI499217, AI419514, AI583289, AI584091, AI423406, AI215005, AI656517, AI659148, AI638551, AI267330, AI291604, AI589198, AI522113, AI538417, AI611454, AI612785, AI767364, AI783468, AI784272, AI818454, AI818461, AI823506, AI866880, AI867959, AI871322, AI935700, AI934160, AI970235, AW015075, AW088209, AW074345, AW074385, AW075425, AW151038, AW236437, AW242817, AW243366, AW272280, AW188817, AW078860, AW292200, AW627630, and AW630913.</p> <p>AU117722, AU117639, AU125461, BG257346, AU125320, BG259614, AL041666, AU134919, BE887285, BF340359, BE270501, BF971008, AU125165, AA593983, BG254919, BG119566, BF791982, BG027717, BG117307, AU129485, AU128253, BF673138, BE410718, AW574556, AW500522, BG177695, BE797876, AL040633, BE770449, BE770431, BE736836, AI742708, BF978550, AI767520, AI742404, BE504225, BF111089, BE910115, AI681786, AU127139, BE545374, BF516249, AI908291, AU152319, BF056960, AW055010, AA126621, BE781576, AI333650, BE467323, AU144420, BF575212, AW996837, AA702137, AA206018, AA701911, AA126494, BE672572, BE737023, BF185788, BE789485, BF978567, AW602159, BF736100, BF820317, AI803067, N36960, AI088039, AL046313, BF132901, BF735867, BE707249, BF477588, AA024996, BF216802, AI912291, AI394065, AI805781, AA887081, AW029557, BF791743, BE217919, BF212498, BF736081, AI376119, AA868717, AA121662, BF898020, AA526920, AI435569, AI075870, AA450145, AI436181, AA889549, AA548268, AW674271, AI636640, W58617, W58616, BF221495, AI686830, AW236479, BF244753, BE502359, AA255800, AI417171, AI916972, BE677826, BF035948, BF876879, BE694966, AA835638, AA447229, AA926978, AI208286, R95825, AA133188, AA609764, BF735994, AA558595, AA663764, R95776, T31467, BF475395, BF571998, AW401693, AA450088, BF736109, R83440, H54350, BF759908, AA972925, AW268985, AL041665, AW674569, BF029677, T06718, AA847564, AW996718, R19916, R67673, AI701761, BF977723, AA641688, AI707476, AW008306, AI749513, BE695062, AA332616, AI248393, BG260186, H53515, AA872693, H21971, AA732501, AI936949, AI093590, AA987830, AV654826, BF210714, AA872122, AA336781, AI379404, BF575890, AL039844, BF571552, H54140, AA025231, AA135593, N46277, N44961, R45136, AA361881, BF063891, Z43024, AA206243, AI570851, AA334590, BE148526, W60520, BF897472, AW674396, AA025992, AA885215, T19008, AW366176, BF910491, BF224308, BE731752, AW263468, AA171577, BE835030, BE080810, AW470374, R50245, Z39126, R66073, H53885, BF812753, AW361717, BF741506, W56208, BE409150, AI572255, AI123071, AA328659, AI003177, AA311578, R55217, R55214, AA630696, AI967952, AI560080, AI691108, AW998198, AA133216, AA135680, D19755, AA027062, AU127146, R34179, AI537428, BF821498, BF931991, AA101379, AA024952, T10703, AW129393, W21413, BE042729, AA235267, N93581,</p>
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HOPKC80	878	105817 4	1 - 1490	15 - 1504	<p>R34301, BF736040, AA026853, AA285351, R55216, BF825296, BG114664, U66615, U85614, A21853, AA780983, AI885909, and AW149246.</p> <p>AI148864, BE673121, AW080794, BF036486, AW170514, AW006431, AI188759, AI832265, AW001480, AW471370, BF439239, AW168034, AW129649, AA769641, AW172714, BE867358, BG251850, BF516562, BE869511, AI598083, BE512714, BG250319, BG248190, BE740431, AA552439, AI587171, AI151456, AA151778, BF229956, AI684150, BE612973, AI339143, BE962486, AA621571, AI221080, AI279608, AW818139, BE868659, AI347951, AA512993, AI471439, AW243807, AA627704, AA973368, AI346482, AW952945, AI050852, BE742221, AA194025, AA410196, AI262321, BF333880, BF034695, AI829191, AA808606, AI344709, AA832492, AI984534, AA149786, AI189417, AI446633, BG251275, BG248564, BE280342, AI828290, AA580361, AI206376, AI924092, T98835, AW273245, AI300760, BE617957, AI271915, BF037659, AI133687, AI074095, AA659629, AW450853, W07258, BE872881, BE617516, BE613433, AI435798, AA976596, AA603691, AW292998, AI950654, AA875879, AI244806, N29871, AA948384, AA946812, AA862576, AI804146, AI982855, AA812251, N79741, AA888824, AI832503, AI133726, AA577501, AA297383, AI220826, BF824752, AA297386, BE963095, AA535896, AW571512, H95187, AA287234, W79526, AW190388, AA631290, AA908173, AA872504, R47933, AA496489, AI301669, AA427910, AA297379, R69472, AA284504, AW004671, AA746077, AA989485, T98916, BE074801, AA487702, AA297484, AA297153, AA464649, AA292774, AW170481, AI963760, W79558, AA394263, AI986058, AA903542, U46323, AW079683, AA487488, T98961, AI342966, AI982682, BF764771, AA287210, BF766656, BF749186, AA297527, AW845358, AA861541, AA297453, AA557937, AI133595, AA464548, AA553875, AW844388, AA486446, AI275661, AI719497, AA496440, AA481372, AI673125, AA565649, AA341051, C21003, BF801101, AA428283, BF512723, BE541671, BF761672, AA298491, AA421514, AI749779, AW007555, AA411012, AI273816, N57294, AW997921, BF763464, BF854746, AA133686, AA411355, AW841964, AW578145, BF743003, T53668, AJ011497, AX013131, AC003688, AF087825, AK026651, AP001726, AL137550, AB052191, I89947, AF069506, AL137480, I48978, AF159615, A70386, AF102578, A77033, A77035, A08910, A08909, AB047904, AK026408, AF130100, AF116631, AL050024, AF232009, X83544, AL049347, AL137459, AF177401, AF287051, AR038854, AF026816, AK026744, AK027164, A08913, AF116646, AX020124, U73682, AK025435, AF130099, AL110280, AX026824, AX026823, A58524, A58523, AL122110, AF130055, AF183393, Y14314, AL117435, AK026462, AK000614, AF116688, AK027096, AL080159, AL389935, AL035458, AL122050, AF225424, AF124728, AB047631, U80742, AL137548, Z97214, AL137539, AF087943, AK027173, AL117457, AR068753, AL137533, AR034821, AF130089, AK026534, AF113019, A07588, S36676, S83440, E02221, AK026464, X82434, Y16645, AF116609, AX019230, AL133113, U35846, AL389982, AF119899, Z82022, AL157431, I25049, AL353940, AF185576, AL080126,</p>
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HPCTP25	880	105828 7	1 - 2729	15 - 2743	AB047904, AF090903, AK026506, AF146568, AL122093, AF081195, AX026824, AX026823, AL080124, A58524, AB034701, A58523, and AK026452. AU119788, AL527530, AU133453, AL041710, BG254929, AU135809, AU125732, AU133490, BG167820, BF980151, AU117705, AU135011, BG177432, AV728081, BF340124, AU142970, BE904257, AI683356, AI718805, AU129705, BG253192, AU136035, BE879896, BF310336, BE876423, BF793406, BE897590, BE313976, AA523878, BG120959, BF576338, AL041709, BE644637, AV653774, BE550211, BF681197, AI627660, AI174799, AA599054, AI022796, AV655073, BE545921, AU150476, BE886184, BF733143, BF979534, AL041354, AU151780, BE669848, AU146044, BE731723, AU160149, AW992165, AW090741, BE467630, AI929634, AW675271, AU144468, AU128178, BF000640, BE465418, AI373094, AI754961, AW206048, AA283346, AI912769, AA305319, AI334432, AI950173, AA010981, AI525702, AI634657, AI096502, AA136982, AI041563, AU156300, AI810295, AW024236, AI080215, W03757, W07811, AI263861, AI266121, AW139644, AA137108, AA010649, AA280680, AI431611, BE178646, AI422044, W16729, AI278157, AI253137, AI276543, N79441, AA722649, AA506701, AI379878, W02153, AA773825, AA113143, AI985396, BF244725, W32487, BE873388, AI954599, AI247192, AV650176, AI400581, AU149335, AA996276, T29823, AW377743, AI300404, AA312038, AA283267, AA456000, AI222171, AV687488, AV684077, AA743477, R99135, AW207341, AA113060, AW244164, AI018287, AW361239, T40919, AW204287, AI275171, AW135486, AA715236, AI193809, AI085593, AU155764, AI810430, AI263461, AW377722, AI378460, AA640240, H48435, BE243042, AA355196, AW998778, AA371081, F11184, AW370196, N90128, AW998780, AA348183, AI436088, C02060, AW377746, R46816, AW998880, BE178988, BE29721, AW900019, BE178955, BE048812, T96654, AW900068, AW900015, BE005744, BE178985, BE178946, AI954168, W31460, AI913558, AA626107, T39968, AI018721, AW892371, AI872850, BF435456, AW998883, BG013386, BE931863, AA233327, BE836418, BE005607, AI095067, AW294149, AW998883, AA092224, BE935313, T96769, BE710361, W31779, N79240, BE817034, D79934, AW377502, BE935425, AW673040, BE935388, BE935582, BF911102, AA233328, BE935510, AI689307, AI866324, BE180359, AW337837, AW512945, AW779517, AI400547, BF093371, BF095040, BF094192, BF672187, BE707372, AW992130, BE242425, BE940388, BF965040, BE172986, BF887652, BG118789, AW627801, AF172093, U34252, U50203, X75425, AF170918, AF170919, and AA650519.
HODKM52	881	105830 5	1 - 1396	15 - 1410	BE675862, AW170492, AW615410, AI921484, AW778984, AI087865, BE504781, BE501303, AW664137, AU804599, AI761680, AW438623, AA564397, BG009559, AU148656, AU155012, AI473829, AI361784, AW082773, BF836752, AI804809, AW854134, AI126258, AW438975, AA053738, AI885468, AA219424, AA053218, R81717, AW951339, R81716, AA639617, R22820, R21206, BE246692, R81678, AW291929, AA829675, BG015493, H53703, AI336922, H53702, AW262475, R81677, AA496643, H43599, BF851318, BF886577, AA298439,

HCONB89	882	105831 6	1 - 2428	15 - 2442	<p>AI691143, BG059519, AA742704, H44640, AA010106, BF747278, BF510615, AA010229, AW373947, AA299976, AW748056, AA159086, D43772, AB008789, AF190121, AR060002, II3162, AR028477, AB008790, AF274875, and D87513.</p> <p>AUI33486, AL531664, AL531663, AUI33130, AUI39013, AUI41515, AUI37644, AUI37574, AUI20996, AUI36221, AV733714, AV715795, BG169581, AUI27912, AV718227, BE783774, AUI38115, AUI37614, AUI38855, BF339894, BG260734, BE891527, BG110089, BF966675, BG171662, BG170082, BE782211, AUI35005, AL039207, AUI34723, BE879634, BG165755, BE895932, BG167846, BF793180, AV726888, BE890841, BG169975, BF363417, AL048640, AUI35846, BG105608, BF571125, AA527272, AW237266, BG115365, BE893637, BF978315, BG171140, AW237326, BF691407, AW027071, BF668607, AL037862, BF363427, BF075327, BF363421, BF669850, BF212851, AV713984, BF363418, BF363425, BF363422, BF691697, AI934569, BF966483, BF031324, BE564631, BG026587, AW089586, BF363423, AV730222, BE893556, BE968638, BF373083, BF363419, BF978056, AA220921, BF363414, BE567768, BF698264, BF389151, BF363412, AV730226, AA664155, AW303541, BF381806, BF701422, AA209438, AA220916, AUI37868, AUI54130, BF363426, AA476548, BF382463, BE968837, BE568406, BG259559, BF373099, BF248406, BG166999, BF363408, AW590404, BF351702, BF208023, AUI46912, AW264406, BF373117, C18982, BF572761, BF678349, BF363411, BF363416, BF383061, BF570658, AA220924, AI422877, BF673996, BE895525, BF694282, AUI53701, BF571324, AW949610, AW475045, AA218949, AA099110, BF243849, AI439160, BF363409, BF695133, AUI30705, AUI54514, AW338521, BF205387, T57743, AUI52609, AV703087, BF693329, BF691506, N42342, BE644934, AW263656, AUI57350, BF373107, AW182386, BF082041, AI096608, BF196144, BF673006, BE175494, AUI51511, AI685369, BF373100, BF692184, BE176777, AA890477, BF373109, BF029724, BE167238, N20605, AI825979, AUI57245, C05885, AUI32632, AA219758, BF571942, AI909012, BF352283, AA604911, N22746, BF373119, AI951164, BF373102, BE972577, BF436503, AI343970, AV725554, AW592381, BF373074, AI492929, AA219755, BG000230, BF373112, H80206, BG007213, AA542825, C04448, W44600, BF571043, AW473983, BF373076, W70075, AI089376, T33636, AI571938, BF373118, N33364, AA534919, AA564819, AI096622, AI539176, BF373115, BF132073, BF373077, AI304768, AI680346, AA147100, AW167191, AA559033, AI346610, BG000231, AW967267, BE166365, AUI50301, BF332576, AI281046, C05238, AW366325, BF218529, AI359688, AI356805, AW191042, AUI55760, AW241669, AW237334, AA216693, AI809362, BF572538, BF373090, AI040424, AA209363, BF433307, AI884545, AA243961, AV716729, BF373116, AA169399, AA961204, BF373114, AUI38282, AW630761, BF363413, BE168800, BE567852, AI695195, AI935419, BE168801, AI037863, AI311119, AI538044, AK025732, U47674, U70063, AF157500, AF220175, AB020867, AB020868, AF220173, AF220172, AX047063, AX033851, A84916, AK025211, AR070327, A62298, AR018138, AB028859, AJ132110,</p>
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HSAB144	883	105841 3	1 - 1580	15 - 1594	AI193089, BF792867, BE275240, AU118203, AI193092, BE740143, BG036632, BE789430, AI826251, AI889985, AI336202, AW189142, AI870838, AI636431, AI889260, AW954406, AI811512, AI684172, AA243747, AI051342, BF058568, AU144830, AA434509, AA456259, AA243853, AI185725, AW662364, AA398605, AW316764, AA622033, AA454646, AI361613, AI123201, AA908199, AI080671, AI886632, AA429015, AA779359, AA232992, AA393244, AA457122, AI051169, AW630662, AI921539, BF446979, AA903191, BE856656, BE207591, AA622055, AA434412, AW390122, AW243723, AA527081, AA429166, AA864257, AI366506, AA125744, AU156496, AA233296, AA908751, T62568, AA535862, AA644355, AW291837, AA631667, AL513838, AA468584, AA678878, AW873708, AA782659, AI274736, BF675160, H16143, AI078706, AA099514, AI084292, BG152777, AA628017, T29605, T63190, H59746, AA125865, AA639563, AA479617, AA476989, AW605918,

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HBPND88	884	105843 2	1 - 1654	15 - 1668	

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H6EE005	885	105843 8	1 - 2416	15 - 2430	<p>             AU141541, AU142138, AU120651, AL516604, AU125809, AU133877, AU125599, BE891465, BF970142, BG259581, BF795463, BE873086, BF347915, BE883289, BE019035, BF314638, BE885433, BF306026, AA702164, BF306818, BF034844, BG107555, BE389518, AA001233, BG027456, BG105546, BF736596, BE313440, AW976026, BE017961, AI921716, N58476, BE313783, AI922691, AW341468, BE781950, W52817, AU149400, AU149229, BE295775, BE207816, AA983287, AI688164, AI798829, AA676905, AA748673, AW769397, BF431049, AA580477, AW261835, AW020522, T03435, AU146658, AA031269, AA811284, AI470013, AL516603, AA553821, AW468092, AU155046, N31376, BE301482, BF248376, AW473322, AI040689, AA203586, W67599, AI308113, H14111, AI369176, R69536, AA069390, AI223241, AI081505, AA954674, N78065, AI184844, BG119995, AI084955, AA634485, AI858188, AI240972, N24082, AA227367, AI220515, AI207036, W67600, AI278789, H95812, BF920571, H72498, AI016960, BF920573, AI206577, BF125563, AW016403, AF202355, AA989138, H24195, R87799, AA889751, AI079252, AA235634, AI862906, AI129076, AI660980, AA995470, AW953096, AA864442, AW182940, D29420, AW089244, R13771, BE871844, AI762381, AW264543, R67168, AW996210, BE465230, R17270, AA665921, BF758203, T57104, N55702, AA227366, BE892968, AA918086, H72897, AA814465, R87736, AA932962, AA634537, BF816643, AA775542, AW627925, Z43480, AI733574, AI240618, AA907067, AI023689, N58699, AA747793, R14023, AA304890, AI648677, R09214, AI581401, AW085844, BF125551, AA917754, F13715, AI669014, T57172, T90491, T90587, AA324981, R41944, AA353530, AA037879, AA970995, BF687794, BF125635, AA037880, AA716132, R09324, N54187, AA639537, BF929243, H14086, AA323230, AA032267, AV750765, AA032200, AA248850, AA031394, AI921060, BF351737, AI022147, AA250785, N93684, BE171774, AA487552, AA069357, T32756, AW274651, AI932548, BF205711, AA411123, AA248912, AI687158, AA001647, BF834414, AW897716, BG171661, AA872759, AV723204, AV723062, AI096771, AI538885, AA862606, AI538764, AL117423, AK023318, Y17711, AK022697, D17220, AK026784, AK027114, AL049430, AF130110, AL133560, AL137258, AL137254, S83440, AB048975, AL389947, AX015416, AL110228, AF106657, E01573, E02319, E06788, E06790, E06789, I77092, Y09972, AB032264, L04849, and AK027181.           </p>

HFIVR61	886	105845 1	1 - 1245	15 - 1259	<p>BE619810, AI735329, AI085963, AI824041, BF110737, AI472218, AW966001, BE789809, AV713543, BE440029, BE439832, AI343270, BE789477, BG167627, BE787841, W51812, BE619489, BG166361, AA721478, AA947476, AW134706, AI095255, AI074123, AI751500, BG248813, AI632696, BF244246, AW300992, BE812262, AW243012, BE786701, W31016, AW630744, AA911581, AI751501, AI868566, BF357224, T92234, BF850452, AA381568, AA381892, AA380919, BF055507, BF432743, AI692513, AA043789, BG029815, R73718, AW630409, AA362308, AW961569, N98983, N98591, AW059879, C21585, AA381453, BE619286, BE619899, BE964153, BF927424, AI539260, AI440238, AL514717, AI539800, AI866469, BE879000, AL513901, AI859991, AL515113, AI828574, AI926593, BF811804, BG258511, AI866691, AW162194, AI582912, AI440263, AW117629, AI889191, AI491710, AL514951, AL513755, BG253986, AI539771, BE897632, AI432644, AL524449, AI537677, AI494201, BF812963, AI804505, AI500659, BG170937, BE883591, AI866465, AI815232, AI801325, AI500523, AI538850, AI887775, AI582932, AI872423, AI590043, AI923389, AI284517, AI500706, AI491776, AI445237, AI289791, AW151138, AI521560, AI889189, AI500662, AW172723, AI284509, AI538885, AI889168, AI927233, AI866573, AI633493, AI434256, AL515307, AI434242, AI805769, AI888661, AI500714, AI284513, AI888118, AI539707, AI285439, AI436429, AI355779, AI623736, AI889147, AI581033, AI371228, AI440252, AI431307, AW151136, AI567971, AI866786, AI860003, AI610557, AI431316, AI242736, AI887499, AW151979, AI539781, AL514887, AI702065, AI885949, AI285419, AI559957, AW089557, AI521571, AI469775, AI866581, AL514791, AI567953, AI815150, AW074057, AL513913, AI446495, AI867068, AI225248, AI698352, AI282268, AL514773, AL514455, BE885490, AI476086, AV729934, AI440260, BG252929, AI955441, AV758217, AI924051, BG251076, BE780932, AA888196, BE927753, BF814072, AI561170, AI554821, AI890907, BF811802, AI804531, BF815930, BE927746, AI690946, AL513961, AI648567, BF812438, AI371251, AI567993, AI866510, AW951463, AL515373, AI433157, AI909641, AL514793, AI225000, AI866461, AI923046, AI431238, BG260287, AL039390, AL514469, AL047422, AL040459, I08633, M18403, M54894, X04403, E01518, X04602, E02930, A10873, M29150, E03737, M14584, A09363, E01616, Y00081, U12234, M86722, AB000554, M80258, S56892, A93715, A93714, A93806, I08634, A38783, I52043, AF014510, E02172, E02170, A93807, E02205, L26028, A42034, A51824, A00344, A00344, AR064654, A57723, X57317, AR075390, AF097323, AF097322, A57729, I27634, I27635, I27636, X62501, AF014505, I27637, I24679, I24682, I24680, I24681, U64794, L46803, AF012908, AK002126, AK002124, AL157483, AB046636, Y14139, AF122896, A51825, A51826, AR064656, AR021249, A42036, AF131773, AB049880, AX046458, AX040958, AX040974, AL122110, AL133070, AL133113, E13998, AL133049, U30290, AL133053, AK000718, AL122116, AL122101, AF119908, M85164, AK024978, AF002985, X97332, AR034821, E12747, and AW134707.</p>
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HVV/BX28	887	105845	1 - 2053	15 - 2067
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HVVBI38	888	105847 5	1 - 2534	15 - 2548	AI038982, AU117056, AU138301, AV700249, AU139391, AV700023, AI742402, AW475039, AW152006, AV656228, AV652168, AV659216, AW512274, AV699449, AA425660, AV658378, AV719940, AI148538, AV696859, AV658729, AV683599, AI636337, BE349130, AV720627, AI924886, AV700643, AV718906, AI922771, AV699730, AV696271, AV699376, AA909379, AU143982, AW880514, BE971470, AW262765, AI814675, AA906235, AV695490, AU144025, W72541, AI086285, AI004263, AI686878, AV699569, AI128250, AI609938, AW514490, AV700045, AA777373, AI142452, AI093128, AV720368, AI352388, AV718583, AV691336, AI921912, AA022784, AI400079, AV719717, AI274261, AV719352, AU157555, AV658403, AV719770, AA573463, AI568119, AV699644, AI151165, AA427785, AL047363, BF906603, AI140357, W88788, AA703392, AI075816, AI190663, AA022691, AV719256, AA705945, AI934030, H29609, AV682135, AI301649, AV658213, H29698, BF221955, AU133483, N25878, AV682117, AV699169, AV700037, AV658253, AI436162,



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HUKEJ46	889	105853 9	1 - 1602	15 - 1616	<p>AW874247, AW874371, AA910550, BF434085, AA534811, AA983386, AU126641, BF757483, AI955581, BF755328, AI672883, AI586988, AA057145, T25016, AA974281, BF758100, AA887124, BF757704, AF081512, AL117348, AF081513, U81523, D83921, AJ000082, AJ000083, AF081507, AF081511, AF081504, AF081508, AF081506, AF081505, AF081510, and AF081509.</p>
HDFTT47	890	105858 8	1 - 795	15 - 809	<p>AI583173, AI473685, AI990953, AI680405, AW575343, AW951299, AI686920, AI279118, AI866763, AW273252, AW262003, AW083564, AW152078, BG236446, AA552648, BE876810, AV714299, AA903579, AA410919, BG230769, AW148673, AW575939, AV752077, AW392557, AI687988, BG235997, AA595644, AW406669, AW578510, AA576706, AI275169, AW950371, AI817519, AI627978, AW118007, AW170604, AI798555, AI287852, AI250410, AV733177, BF087348, AW082656, BF663857, AI439674, BG058620, AI956001, AW263617, AI381595, AI362475, AA224990, AI356365, AA961950, AI735409, AI733503, AA225038, AI829822, AI308923, AI004331, AI476133, AA576297, BG012427, AW406548, AW193241, BF128864, AI829843, BG176760, AI242627, AI537866, AI281599, BF737111, AI792212, AI572936, AI708910, AA458472, T28167, BG012426, BF843204, AI675832, AA871998, AA669055, BF924288, F26079, AW571413, BF844800, AI758642, AA954889, AI275200, AW189214, AI432217, AW169616, AW380025, AA442984, AA258595, AW795512, AA258624, AW407966, AW795511, AW391063, BG009113, BG149250, AW872490, BF737114, AW952175, BG012425, AA406361, AA406417,</p>

					AA029822, AW406195, AA029823, AW270582, AA564154, N39759, AA478213, AW406248, AI865338, BG024731, AA740313, AA939204, R73128, AA430464, AA366866, AA478051, AA642383, AA961824, N26316, AW589207, T79121, AW798302, BF924284, R73184, AA320518, BF092132, AW882104, BF853762, AA434515, AW374085, AA215608, N76616, R19164, R01628, BE220959, BF238125, BF334673, AI349106, H43204, AW238660, AW296828, AW796748, AW404774, BF572262, AA809121, AW406568, BE810479, AW405158, AW006264, AA434417, BF976441, AA479841, AW151357, AI691004, BE171122, AI805742, AW882292, M60028, M32577, M24364, M81141, M57650, M57649, J00198, M16276, M17563, K01499, U92032, M17564, X03068, K02405, M81140, M20505, X00369, U83582, X87344, M17955, M33907, M20432, L33910, Z80898, L34096, AF195245, L34097, L34098, X76553, M35730, X76554, M20332, M20333, U66400, M16996, AF037315, S53999, L40179, L34095, L34099, L34100, M15809, M35731, L34105, L34106, AF000447, L40181, L34104, U83585, L42626, L34107, X96420, AJ223253, L34101, S40629, L40180, L34103, L34102, AF043908, Y18202, M90802, Y07947, Y07946, Y07945, M90804, M90803, M90805, AF043168, M33307, M25025, X56596, U65217, M15355, U65218, M36151, M21932, M13538, K00115, U39089, and M60562.
HSSFS71	891	105859 6	1 - 500	15 - 514	BF309366, BE908964, BG030274, BF529310, BE906932, AL524107, BE899502, BF207110, AL524321, BF206454, BF314425, BE410188, BE387063, AL519836, AL515731, AW163247, BE207049, BE298771, BE313315, BF032587, AW163135, BF036749, AW966563, BE612399, AW966557, AW583813, BE386128, BF219994, BE910307, BE383711, BF701280, BE612672, AW583752, BE729998, BE385039, BE383977, C17895, BG030571, BE615838, BF037714, BE741510, AW247611, AI878890, BF343434, BE21979, AA459193, BE736474, BE384598, BE737190, BF348206, AI815391, AA136110, AA481716, BE391879, AI751884, BG254389, BE789300, T33372, BE744046, BF315514, M78227, AW002542, AA397605, BF308141, AL038945, AA045714, BE395307, AL519835, H38469, H15232, T09997, AL524106, BF305982, T08625, BE909139, H18019, AW160802, AW249946, T34483, AI932344, T78291, BF339698, AA121099, H11912, H42617, AL524320, R90886, R85161, BF436417, F05361, AL536167, BE909379, BF847828, AI871752, BE669457, AI420118, BF448303, BE670936, AI887806, AI690297, C05027, AI307794, BE613278, R13703, R53244, AW732277, R54155, AW002869, R00683, AA485591, AA905687, BE620961, AW246212, R35117, BF772134, U36190, D42123, and D17512.
HSDJH63	892	105861 2	1 - 1500	15 - 1514	AA741118, AW451491, AA252360, AW975618, AV718489, AW966053, AW978634, AW960553, D80253, D80188, AV722801, AV699447, D51423, AV724520, AW966531, AW966534, D58283, AV719557, D59859, AV699550, D59889, D80166, AW978661, D59619, D80210, D51799, D80240, AV719822, AW949645, AV718692, AW973307, AV719324, AW965177, AV720211, AV720731, AV723927, D80212, AW949656, D80227, D57483, AW949642, D80366, D80195, AW975621, AW959570, D80219, D81030, AV718440, D80391,

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HAHGD24	893	105862 2	1 - 1314	15 - 1328	<p>AR066490, I14842, I18367, D50010, A63261, X64588, AR016691, AR016690, U46128, AR008408, AR091537, AR062872, A70867, AR093385, Z32749, D13509, A64136, A68321, U79457, AR060133, AR087528, I79511, U87247, S69292, AB023656, AF123263, AR032065, X93535, and AR008382.</p> <p>AI935823, AW664925, AI805549, BE677483, BF109878, AW262864, AW300962, AW008229, AW167386, BF197239, AI857550, BF341458, AW572485, AW493971, AI805365, BE221220, AI554583, AI953162, BF032290, AW089913, AW952401, AI638571, AW675600, AW104806, AA434376, AI467884, AI673775, AI740642, AU149181, BG178196, AI680267, AI936312, AA430337, AI623857, AI184933, AI017079, AA664357, AI682694, W72320, AU154874, AA459289, AA428381, AI453624, AW167276, BE856447, AI026737, AI682932, BE220921, AA305589, W67797, AW139650, AW629990, AI536942, W67855, AI270292, AW175941, AI860034, AV655526, AW084313, AI364650, AI798284, AI886607, H28992, BE736139, AA430385, AW105495, AW080666, AI955970, AW016122, AA746169, AW576533, AI434880, AW262874, BG058348, AA427358, AI915650, BE873341, BG012721, AI339382, AI368547, BE909112, BG261315, H02204, R70310, BE046185, AI472500, AA614143, AW305152, BG056333, BE542123, AW613789, D29029, BE563107, AI914675, BF038706, AU133623, BE093293, AW975037, AW975965, AW971403, AW976024, AW975031, AW969791, Z99396, AW972845, BE737406, AW972292, AW975628, AW979204, AW979127, AW971975, AW974801, AW975002, AW969680, AW975032, AW976023, AW979002, AW877209, AW969643, AL119324, AW975952, AW969673, AL119457, AW974786, AW973717, AW975966, AW975971, AW975154, AW971326, AW971968, AW979238, AW975032, AW975025, AW973213, AW975981, AW975959, AW979176, AW975105, AW972680, AW975954, AW972296, AW971375, AW979106, AW979090, AW971378, AW972721, AW969885, AW973209, AW979098, AW973219, AW975930, AW975942, AW974823, AW970942, AW975027, AW974975, AW975254, AW979134, AW976982, AW975020, AW973750, AW969839, AW970936, AW971732, AW975019, AW971404, AW974785, AW970969, D45760, AW979169, AW974998, AW974964, AW970889, AW974658, AW974806, AW979294, AW969816, AW975876, AW969852, AW972684, AW976031, AW976511, AW979054, AW975028, AW975157, AW975022, AW972377, AW969637, AW970010, AW973812, AW972849, AW979076, AW976000, AW975692, AW972817, AW974802, AW973810, AW975585, AW975015, AW975649, AW974338, AL119399, AW979037, AW972867, AW973270, AW970113, AW972154, AW972884, AW973202, AW972695, AW973805, AW972719, AW976515, AW975976, AW979165, AW976510, AW971387, AW975975, AW973770, AW969884, AW972943, AW969759, AW979083, BF592735, AW970587, AW973650, AW979175, AW973986, AW979064, AW975938, AW975016, AW975138, AW975968, AW970921, AW969766, AW979116, AW975244, AW972806, AW973987, AW975910, AW975943, AW972689,</p>
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HTAEV85	894	105872 3	1 - 3249	15 - 3263	<p>AW972706, AW973164, AW970097, AW973824, AW971964, Z95636, AB011105, AL354836, AX046357, AR060234, AR066494, AJ279014, AR023813, A81671, AR064707, AJ251859, AX030435, AR069079, AR096545, AR054110, AB026436, AR096546, and AI582832.</p> <p>BE743925, BE743575, BE378832, BE562723, BE294053, BE394456, BF795479, BE388681, BF037525, AW607813, BE855547, BG235939, BE742475, BE378447, BE395372, BE379289, BE395340, AA399317, BE394992, BE350066, AW269658, BF033725, AV721020, BG057713, BE855481, BF941362, AW071828, AI672782, AI589288, AA635623, AI952009, AI553739, BF874688, AI524197, AI333826, AI809288, AI051257, AI423403, AW444587, AW404848, BE670760, AA814571, AI221743, AA291537, R58899, AI829285, AI418846, AA806818, BF953369, AW576501, AA084339, AA420642, AI953273, AA378569, AI356753, AI953017, T33610, AA350904, AA912707, R55664, AI024694, R90802, AA323883, AI372418, T33644, AI797874, H17555, AI339970, BE394689, AI985914, AA894697, AI350316, W22337, T16022, BE392352, AW085823, R88491, AA910596, AA815454, T33681, AA628149, H17451, R90803, AI627590, R55665, AI372419, AA326015, AA813547, AI356317, AA021487, BF920676, AA776204, AA953514, AI391714, AI887011, AA678937, BG152477, AA296883, T30918, T30945, AI372421, AI372420, T33218, T31286, AA350810, AA323752, T33219, T30906, AA782949, AI655347, AA493844, AA341681, T03448, AI024341, AI014310, AA398230, R43882, AI886803, R66432, AA805970, BF921111, AW518669, AL041008, Z42334, R52818, AA080905, AI475040, R19528, AA404699, AI815069, AA324503, BF929916, Z38828, T59381, T33680, AI919449, BF830756, AA325142, H50012, AA341603, BF947931, F01860, M78925, AA323277, BF924567, H15894, BF919142, AI015469, BF881778, AA323721, BF919066, BF918558, BF808617, BF847205, BE673584, AW378345, BF803820, AI740981, Z42668, AI918282, AA019030, BF089820, BE698940, Z42460, AA021656, R52857, AA988658, AI025132, BG150860, AA019306, AW952342, T06612, AI525653, D87465, and AC022392.</p> <p>BE779992, BG177813, BF765915, BE541570, AW971745, AV645385, AV681500, AV645390, AV645392, AV645393, AV681492, AV681509, AV681529, AV681512, AV681526, AV645336, AV645317, AV681507, AV681465, AV681525, AV681495, AV681505, AV681502, AV681504, AV681486, AV681483, AV681464, AV681462, AV681487, AV681506, AV681523, AV681519, AV681497, AV681471, AV681527, AV645404, AV645401, AV645332, AV645383, AV645377, AV645379, AV645389, AV645369, AV645380, AV645321, AV681501, AV645400, AV645353, AV681458, AV645334, AV681510, AV681528, AV681474, AV681514, AV645339, AV681477, AV681491, AV681472, AV681475, AV645358, AV681488, AV681513, BE613349, BE612945, BE622828, BE613070, BE614307, BE613136, BE614237, BE622931, BE621911, BE614230, BE622925, BE618811, BE622868, BE620742, AV681461, BE614451, AV645350, AV681531, BE620756, AV645344, AV681468, Z99396, AW804686, AW392670, AW861944, BE695785, U46346,</p>
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HSPSG28	897	105897 7	1 - 1786	15 - 1800	<p>AL523674, AL521887, BE729929, BE795619, BE735422, AA642486, BE796087, BG032524, BE902739, BG249231, BF568226, BE727596, BG029666, BG035352, BG252593, BE746406, BE880141, BF569176, BF981181, BG163896, BF791978, BE730608, AV711309, BG251203, BE619285, BE893752, BE622769, BE777976, BE733143, AV709554, BE619898, BF026170, BG179649, BF345713, BG024975, BE622470, BE885739, BE745793, BG117791, AU138905, BF026874, BE892012, BG030285, BE901017, AI568349, BG033547, BE407503, BE739907, BE271557, BE893682, BE262240, BE262163, BE885724, BE729340, AW006368, BE535940, BF313089, BE897584, BE896150, BF035839, BF973744, BE259728, BE383334, BE737384, BE263835, BG112438, BG122657, BE409679, BG117040, BE314351, BE296120, BF313041, BE276437, BF220035, AI026671, BF184610, BF940069, AI660276, BE388810, BF672342, BE384006, BE407397, AI571309, BF316322, AI568351, BE727893, BG120531, BE222588, AA677667, BF219961, BG254426, BE259578, AA512929, BE674818, BF668725, BE397144, BE272258, BE294602, AW732380, BF982474, BE261035, BE388998, BF129014, BF245599, AW250102, BE858172, BF540723, BF032578, BF219325, BE886030, BF125719, BE538580, BE311522, AW103429, BE742175, BF035559, AW044691, BE731056, AW247844, BF590637, BE260154, BF540719, BE294673, AI207915, AI204248, AI352696, BE265926, AI394268, BF035929, AI123366, AI040954, AI217608, AA621702, AI459023, AA969486, AA215793,</p>



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HTGFW12	898	105900 6	1 - 2883	15 - 2897	<p>AB047887, AF091084, AL353625, AL122110, AL133104, L13297, AF028823, AK026480, AL133080, AR072149, AB047897, AK024601, U57715, AL133081, AF155119, AK024545, AL137281, AF090900, Y09972, T94239, T93817, N74293, W73835, AA129159, AA166807, AA659289, AA766427, N86084, R29027, AA181528, AI249490, AI348774, AI216518, AI470727, AI770153, AI953691, AI973195, and AW514118.</p> <p>AU140605, BF568181, BE884933, AI092272, BF114739, BE763779, BF840656, AI831722, BE304459, BG177103, AI147872, AA458667, BF674494, AV655809, AA256169, AI539402, BF697242, AI096500, AA42352, BF381825, AA428236, BE090126, AA151500, BF984173, BF840055, AA282385, BE090067, BF207751, BF529849, BF680924, AI140631, BE675175, AW390677, AW630204, AW072144, BE676031, AI433648, AA256227, AI341574, BE883788, AI610253, D81337, AI351995, AI434401, AA151555, BF216419, AW968473, AA770647, BE041624, H25509, AI027709, AW391345, AA297413, AI014823, BF811216, CI5868, AA199618, AA418026, AA707711, AA076687, AW148510, AA078218, BF766312, AA621085, T93906, AA297224, BF766317, AI274433, BG011908, AI225016, AA411808, BE675201, AA206606, T93863, BF808379, AV752818, AI079394, AA459495, AW901133, AA434457, BE814536, AA782931, AI571067, AI800888, BF889065, AW882790, AA973520, AA740470, AI084443, BE814559, BF096206, AA089762, AI393589, AA917605, AA403077, AW374569, BF351151, AA207235, BE703954, BE718099, BE701207, AI761298, BE703998, BF800704, BF327250, BF766235, AI686835, BE703901, AA776963, AV735938, AA908680, BF847468, BF847463, BE828695, AA437275, BF845178, AA078169, AA282042, BG231225, H86310, AA205333, BE814371, BE147951, AI039733, AI583024, AI192131, AW401404, AI039000, AW151695, AA077054, AW883686, BE701170, AI090090, BE701175, BF829714, AA887635, AI375569, BF364757, BF756621, AI401537, AI520978, BE703999, BE891094, BE932845, AW976626, BF796278, AA161026, BE938866, AW361568, AA013439, AA769612, BE815326, BF822013, AI267887, BE815369, BE163029, BE698283, AA911366, AW058057, AI268076, AU120696, UI13696, UI4658, U28724, AC005995, AB017004, D38435, D38436, U38964, AB017007, AB017006, AB017005, D38437, AC006014, AC005488, AC005071, AC004867, AC005098, AC004166, AC006480, U38979, AC004878, AC018720, AC007000, U38980, D38438, D38440, AC005088, D38439, AC004980, AF030453, AR062818, and AR062817.</p> <p>BE615276, BF340866, BE909308, BE876727, BE878185, BE787546, BF793219, BF025894, BF346288, BF027348, BE907259, BG171700, BE870259, BE793972, AI869324, BG251535, BE905686, BF344721, BE797588, BE539065, BF526208, BF724433, BG260401, BF346215, BE906884, AW068684, BE890682, BE909949, BG178360, N20475, BE392521, BF312304, BE867221, BF026564, AW179034, BE276165, BE276172, BE277237, BE789580, BE062186, BF087437, BF880137, BF311180, AW732268, BF378665, AW884175, BE906327, BE908992, R88501, BG168264, AL045190, AW601604, BF343463, BF569508, AW402407, BF317451,</p>
HOFMT75	899	105905 0	1 - 1485	15 - 1499	

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HARNB17	900	105908 5	1 - 1773	15 - 1787	<p>AI652284, AV699731, AW772193, BE567359, AA948087, AW772160, AW779951, BF061442, AW275997, AW772178, BE501251, AI741087, AW468826, AW504488, BF694626, AA588762, AI650484, BE042660, AW021276, AI453254, AA983512, AV681483, AV681519, AV681502, AV681487, AV681526, AV681512, AV681462, AV681505, AV681465, AV681464, AV645390, AV645385, AV681529, AV681486, AV681525, AV681497, AV645393, AV681523, AV681495, AV681506, AV681509, AV645317, AV645336, AV681504, AI337944, W61302, AV681500, AV645392, AV681471, T93088, AV681507, AI590203, AV681513, AV681492, AI215418, R61302, AI214698, AI380725, AV645379, D62123, AV645377, AV645339, AV645353, AV645383, AV681528, AV681458, AV681477, BE892916, HI1528, AV681474, AV681491, AV645389, AV681472, AV645332, HI0464, AV681514, AW779966, AV681510, AV645321, AV645400, AV681527, AV645401, AV681501, AV645369, AV645404, AV645380, T93181, AV681475, AV645334, N42857, AI084484, BF185904, N40724, W65366, AV645358, AV681488, N33340, N21245, N27958, R44952, AA327161, N34449, C02871, AW971745, T93148, BF243907, H06275, H16402, AV681461, AA598831, BE614237, R81480, AA333901, BE613349, BE612945, BE622828, BE613070, BE614307, BE613136, BE622931, BE621911, BE614230, BE622925, BE618811, BE622868, BE929621, BE620742, BE614451, AV645350, BF034128, AL514919, AL514357, AL514691, AL514627, HI1585, AV645344, AL119457, AL513597, AL513693, AL514087, AL513977, AL514791, AL513907, AL514473, BE620756, AL513553, AL515413, AL513865, AL119399, AL513643, AV681531, AL514543, AL514155, AL513999, AL514063, AL514085, AL513631, AL513755, AL514721, AL514793, BE889755, AL514015, AL513779, AL042544, AL513687, AL515191, AL513817, AL514579, AW877209, BE966443, BE966577, AL513723, AL514823, AL514409, AL514929, AL513951, AI453322, AL514093, AL513911, AL514867, BE966547, BG179099, AL514493, AL514101, BE964994, AI520785, AL513979, AL514657, AI282355, AI564719, AW117882, AL513781, AL514935, AL515235, AW167448, AL042382, AI862139, BG167249, BE966388, BF970652, AL515195, AI366900, AL514457, AL513789, BE963909, AI889376, AL514097, AL513901, AL514219, AL514359, AL513985, AL079794, AI433157, BG179586, AV723772, AL514541, BE886686, AL514025, AL119511, BE962898, AL514983, AV681468, AA449768, AL513809, BE965891, AL514871, AI567351, AL514511,</p>

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HDABR73	908	105953 2	1 - 1682	15 - 1696	AA425390, BE811777, AI630066, BE900769, AA352240, BE528369, AA353182, AW302203, BE696471, AI525367, BF222250, BE646001, AA040074, AI263834, AW190054, BF222563, AC005037, AI158832, AL356244, AP000497, AC002433, and AC025765. AL536057, BE621676, BE741988, AL536058, AU119339, BE744459, BE378587, BE796157, BE378842, AI983859, AI188641, BE747937, BE742130, BF037284, BE740301, BE740930, BE563813, BE315119, BF796407, BF036145, BE563067, BE733406, AI819257, BE793554, BE744012, BE747573, BE271659, BE273401, BE898557, BE741463, BE741182, BE7444371, BE747343, BE740836, BE743761, BE250007, BE740615, BE743726, BE741624, BE612835, AU118578, BE745593, BF036439, BE909331, BE743960, BE563771, BE612827, BE617787, BE741187, BE898606, BF034541, BE736299, AU135570, AW190372, BE906395, BE613272, BE741701, AW024509, AI982697, BE515259, BE906409, BE744503, BF036857, BE744695, BF038326, BE741281, BE515348, BE873534, BG116590, BF036488, BE745744, BE740015, BE612664, BE740873, BF038719, BE379468, BE272232, BE612831, BF035437, BE744260, BE271379, BF035175, BE394400, BE563064, BE315354, BE906753, BE899472, BE378543, AI149550, BE872877, BF035117, BE746985, AA843413, BE906163, BF036589, BF034503, AW583110, BE395267, BE910084, BE515311, BE395315, BE019905, BE271729, BE392414, BE617294, AW276453, BE869007, AW276419, BE515206, BE742967, AI022639, BE870918, BE311817, BE742113, BE867683, AI888932, BF853014, BE315347, BF038858, BF792372, AA779427, BE392271, AW438754, AW629644, BE869063, AI627588, BE899214, BF033988, BG178683, AI186468, BE621326, AI925167, AW168073, AI689311, BE390431, AW275877, BE745272, BE293876, AI684241, AI523546, AI199013, AI797261, BE393953, BF035502, AI140251, BE044623, AI473805, BE392821, BE621075, BE963030, AW167490, BF035223, BE393111, AI684174, BE393141, BE742280, BG106822, BE392012, BF941529, BF038912, AW613339, BE744103, BE514842, BE742664, BG255080, BE315034, BE390824, BE899489, BE613027, BE395645, AI038941, BF854473, AU145103, AA837517, BF116137, AI916679, BF038872, AI679059, AI921137, BE281519, BF032879, AW674573, BE512771, BE743687, AW510505, AI955305, AW131534, AW029106, AA915950, BG180201, AW629761, AI983048, AA866041, AW769050, BE741547, BF038553, AW263798, BE314998, AW088348, AW028733, AI034115, BE379326, AA854434, BE208252, BE736344, BE562631, BF435908, BE613182, AI003490, AW303937, BE293712, AI204099, BE908261, BE315110, AA581854, AA143705, BF036530, AW264648, BF436324, AW105631, AW275263, AW303959, BE742264, AA745970, BE315007, BE378339, BE746207, BF038753, BE389050, AI312907, BG001068, AW058613, BE536750, AW955498, N30199, BE908239, BE873618, AI365005, BF814644, AA845390, BE899025, BF132343, BE562447, BE395651, BE613391, BF804795, AI624991, AW613278, BE834314, BE315002, AB006534, U78095, AF027205, AX014903, AC011479, AR069031, Z36849, AL110280, AF231020, A23630, A65341, E03348, E03349, AK026533, AF090896, AK000753, AF067728, AX042059, AF217982, E12747, AF032666,
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HOGAJ24	909	105962 6	1 - 2068	15 - 2082	BE379134, AI888030, BF128625, BE315492, BE745894, BE466278, BE392102, BF309700, BF090313, AI138758, BF035128, BF947100, BE673650, AW029058, AL119602, BE745470, H14434, BE843655, AA349626, AI372719, AA324193, AW136531, AI492113, AA349625, BF942915, AA324192, H14384, AA323454, BF308236, AW503953, AI372720, BE701341, AA326695, BF928744, AW899391, BF091837, BF129284, BF033438, AI372718, AA019306, AA021656, R52857, BE763486, D87465, AJ001453, AJ278999, and AC022392.
HTJMV05	910	105969 2	1 - 1343	15 - 1357	AL533338, AL533177, BF344698, AI972455, AI474115, AI591062, AI818584, AI201413, AI273898, BG057719, AW518049, AA603336, AV724284, AW473681, AI970058, AI744020, AW950521, AI952552, AV723567, AA732056, BF663206, AI400103, AI675467, AA759046, AI203142, BG106770, AW589861, AI939384, AA291187, AI359478, AI359539, BF871968, AI634408, AA922462, AI890058, BF478007, BF088645, AA641809, AW294543, T28368, AA357035, AI657195, AA356558, BE076268, AA535579, AA284105, AA641772, AL532106, AW849966, L11329, U23853, and AR075978.
HOOIL70	911	105971 0	1 - 2301	15 - 2315	BF976003, BG255591, BE737081, BF128847, BE869747, AI669358, AW574500, AW337117, AI624261, BG236470, AI802759, AW274480, BE872836, BE280264, AI436622, AA777455, AI241448, BE793202, AI214047, AW402432, AA574166, AU154023, BF969067, BE162510, BE901499, BE904079, AI382223, AA877757, AI379692, AI088105, AI079670, AW001896, AI241452, BE280812, BF896455, AA534306, AI274205, AV647149, AA679657, BG231909, AI439904, AA282664, AI656544, AW385182, AI140749, AI372965, AW073615, BF185370, AW402786, BF868702, AI192703, AA482536, AV647081, AW401577, AW406237, AV696093, AA910515, BF851252, AA025527, BF847410, AW073431, N91809, AI797822, D58678, AI491753, AA807121, AA005102, AA594367, AI937299, AA312612, BF868707, AW574667, BF893710, AW408249, AI652285, BF884407, AA641459, BE243024, BE280241, BG059397, AA975471, AI357183, BF662959, AA778878, AW272935, W31243, BF662936, AI247758, AI962576, AI040521, AW372928, AA364415, AA634861, AI570459, T63947, BE242245, BF214009, BF870464, AW518023, BF893670, AA337402, BF762332, AA971623, AW950683, BE513081, BF900388, AI241176, AA806951, BF351083, T28667, AA005103, AA426411, BE697295, AA937746, BE161991, AI907772, AA384860, AA721435, BE832442, T63326, AI123167, BE935009, R15726, BF378229, BF884412, BE832421, AA563915,

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HUNAE87	912	105974 3	1 - 943	15 - 957	BF205763, BE542556, AW602105, AW501478, BE279707, BF734085, AW845227, BE926163, BE241826, BF989806, AI751428, BE242794, AV656636, AA299026, AV656609, BG002474, BF851533, BE383929, BF812975, AL040310, BE185148, BE169980, H57695, T05030, BF084353, AW732695, BF752738, AI703311, BF086412, BE618406, BF814907, AF062336, AF062317, AF062319, AF062320, AF062321, AF062322, AF062325, AF062327, AF062328, AF062330, AF062331, AF062334, AF062339, AF062341, AF062323, AF062332, AF062335, AF062337, AF062338, AF062324, AF062329, AF062343, AB002382, Z17804, AF062333, AF062318, AF062344, AF062326, AF062342, and AF062340.
HTPHO01	913	105976 4	1 - 1068	15 - 1082	BG031300, AU121404, BE745068, AW340658, BF672040, AI830575, BE296082, BF104795, BF205385, AI970997, BF436314, BF436678, AI375239, BF033148, AI955746, W52045, AA452348, AA505698, AA452125, AW403701, BE250987, AI742513, AI199971, AI338181, AI338219, AA926692, AA938400, AA644138, AW402946, AI344126, AI675706, AI300753, AI186703, AI183773, AA156689, BF194804, AA884026, AW938860, W60021, W38892, N95054, AI148098, H01993, AA954291, W44927, BF106195, AA805553, AI751818, AW170013, W39574, AW150567, AI864148, AA280408, AI494112, H04586, R27968, AI193848, AI078102, AI936538, H39712, AI198333, AA194406, AA094826, H02089, BF694536, AA363376, AW959394, AA642334, R28221, T94680, AI373118, AA280407, AA994085, AI352072, AW973632, H13826, AI818830, AA918331, AA554306, AI093632, AI276589, AA447655, AI273430, N30561, H28693, AA134664, AI278504, AW341382, H13182, AI934888, W24049, AW858525, AW861944, AW861914, AW858490, AW858455, AI142134, AW971368, H13867, AW972879, AL134524, AW971207, AW975661, AW970561, AW973817, AW971122, AW975696, AW973756, AW971308, AW979267, AW974137, AW974982, AW975026, AW973721, AW971175, AW970626, AW972839, AW973648, AW975061, AW971296, AW971145, AW979309, AW974123, AW979310, AW971279, AW971339, AW972409, AW975389, AW975999, AW979317, AW971107, AW971992,

HDPWK69	914	105978 4	1 - 483	15 - 497	<p>AW974677, AW974948, AW979312, AW973725, AW974909, AW974885, AW971271, AW972428, AW974896, AW970011, AW975424, AW975563, AW973375, AW979124, AW979222, AW971739, AW972926, AW969869, AW971956, AW971991, AW975887, AW971423, AW972833, AW973739, AW974084, AW971343, AW972743, AW974146, AW970579, AW973783, AW979111, AW971399, AW979122, AW970615, AW970618, AW973265, AW969909, AW972311, AW975852, AW971416, AW971066, AW970597, AW975560, AW970621, AW975862, AW972907, AW971328, AW972148, AW972712, AW976011, AW971972, AW970576, AW971128, AW973143, AW973247, AW974097, AW971315, AW970886, AW976043, AW974873, AW971008, AW972899, AW975383, AW972376, AW979149, AW971383, AW972908, AW976992, AW969851, AW975672, AW971265, AW971300, AW970925, AW971426, AW975222, AW974696, AW969953, AW974706, AW975674, AW975589, AW971033, AW973370, AW974369, AW979112, AW970841, AW973657, AW974661, AW973975, AW974408, AW970541, AW974278, AW970113, AW971313, AW975372, AW972682, AW972932, AW973813, AW974645, AW970563, AW979234, AW972319, AK022176, AF169284, AF216709, AR076513, AC034187, AR066494, AJ276253, AJ276255, AJ276256, A93923, AR096545, D17247, A93916, AJ238010, AJ276251, AR064707, AJ276257, A93931, AJ276254, and AR023813.</p> <p>BE336913, BE735084, BG177051, BG115809, AI201776, AL514548, AI525640, BF205941, BE903276, BE929876, BE312055, BE261573, BF911153, BF911226, BF911152, BE295053, AW411495, BF308316, AA738028, AW403566, AU141467, AU077092, BF683650, BE899583, BE397737, BF982913, BF206934, AW411017, AW245548, AW248320, AW245816, BF987515, AI750480, BF684995, BE614142, BF987508, BE019048, BF850976, W58719, AW246237, BE397252, BE269186, BE267606, BE315417, BE267874, BE513877, BE560286, BE731247, BE797425, BF954541, BE389823, BE391286, BE392270, BF303974, AL515420, BE733007, BE869407, T35777, BE045345, BF528622, BE271945, BE741426, BF987526, H49449, AA581199, BF975243, AL534668, BG163503, BF954542, AW249085, AI750467, BF246555, BE785416, BG025673, BE302637, AL518566, Z44026, BG115160, BE302638, BE410267, BE250546, BG163434, BE871158, AA314558, BE265447, BG251036, BE777968, BE741047, BE873520, BE300463, BE390220, BE277785, BE389706, BE548855, BE407189, BE275582, BE276320, BE274389, BE275212, BE274887, BE796598, BE263988, AW246104, AA852697, AW732316, T35602, BE902471, BE900774, BE733887, AA481899, BF911224, BE892347, BE407783, AL109827, and Z22466.</p>
HPCOK03	915	105984 9	1 - 2056	15 - 2070	<p>AL516768, AL518528, AL516767, AU124034, AL518529, AI038260, AU132739, AU124236, BG168689, AU120266, BG027837, BF965774, BE882118, BE547389, BG027828, BE779679, BF062086, AI126792, AI884785, BE296227, BG250804, AW957623, BE299015, BE785170, AI917458, BG116309, BG110174, AW516673, AI689761, AW732512, BF218050, AA313688, BG108532, BE503915, AU154211, N64029, BF304720, AW409753, AA629662, BG164674,</p>

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HVVBP14	916	105985 2	1 - 2041	15 - 2055	AI458677, BG113558, BG121106, BG171686, AW994500, AV702133, BG117173, BG115089, BG111087, BF343716, BF828843, BF829681, BF337845, BG115532, BE787714, AW606596, AU132146, AU142931, BE537132, BG118340, BF826024, AW069171, AI908290, BG001540, BF574744, BF345139, AI817760, BF680782, AV746169, BF217297, BG164687, AI457607, BF828614, AW384091, BF112151, BE563366, BF540810, AW157443, BF828601, AW157182, BF185879, AV746201, BF816368, BF106026, BF347142, AU117794, AV746339, BF790933, AW026652, BF674283, BF508654, AW604674, BF827085, AW068896, AW172774, AA573787, AW606615, BF525732, BF446072, AI015329, BF826141, AI741571, AV746329, AW261860, AI808809, BE180528, AI809263, AW803964, AI589854, BE621130, AI246006, BF383145, AI638864, BF589354, AI582167, AW995360, BE621552, AV746237, AW117301, AW384072, AW873335, AA191422, AW273374, BE549656, BE504212, BF826112, AI033917, BF930719, AI018004, AW168821, BF816362, BF130935, AI366144, W07385, AW339114, BF223629, BE041847, AW274618, AA480828, AW861537, BF435125, AI689934, BF826149, AI142724, BF245347, BE810306, BE742456, AI672739, BF431193, BF826134, AA041259, BF340103, AA410869, BF814554, AI538338, AI922909, AA114081, BF195307, AU138600, BF816413, BF680922, BF195593, AU137360, AU136469, BE645054, AI527496, AW052081, AW857695, BF112077, C17509, AA209279, AI379051, BF919850, AA446122, BF573765, BE856614, BF229165, AI524734, AA429980, AI086883, AA446430, BE538804, AI936200, AI084992, AA639227, BF084673, AI242682, AU135551, AI081085, BG179108, AA507856, AA976105, AI859258, BF056523, BF247734, AU136580, AI281062, AA933012, AA658931, AW189095, N48334, AA774240, AI299111, BE272095, BG118976, R67390, H04035, BF826806, AV745246, AI368091, AA709018, AA910766, BE877841, BE545689, BF209170, W26396, AI097285, AI681347, AW951203, AW132085, AA181643, AW369852, BF825868,



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HOOJC15	917	105996 7	1 - 1499	15 - 1513	N23036, AW069188, AA312842, BE837689, N28698, AI859142, AU159346, AV714891, AU153662, BE675292, AW965809, AU150988, AW605548, BE965774, AA494486, BF310138, AI024942, AA587968, BF694016, BF111207, AA663127, AI143246, BF891442, AI093098, AI963205, BF969769, BG249168, BE732149, BF031298, AA305846, BF684799, AL521968, W04430, BG028071, W56324, BE732105, AA573252, AW675226, BF345673, AI469839, W56244, AA470048, AA502907, AI674900, AI823838, AA536108, AW337905, N79195, AI378060, BE208643, BE208461, BF973626, C02367, AI085703, BE537520, AA836367, AA416876, AI689700, AW376741, AW505291, BF570805, BF341027, AW363086, BF221634, AA442519, AI371309, BF980019, AA642512, AI954659, BE837802, AA399550, AV652925, BE264023, BE266231, BF754737, AA935807, AW976875, BG027843, BF806676, AW578946, AL515221, AI479754, BF857849, BF806728, AI654305, BE738121, AW970913, BE158832, AA837000, AA744021, BE241611, BE843184, H73550, BE158779, AI792377, AV720699, AV729885, R97239, AL120004, BE314980, BE740092, BE744793, BF991592, BE742591, AA318894, AA516193, AA279385, AA515733, AW897556, BF772490, AI805439, BF771419, BF916935, BF770580, AA209208, AA533054, BF916919, AA669560, T26476, AW819524, AI343169, AA445908, AA070456, H94751, AU118265, AI697425, AK022952, AL117639, AK027026, AK022576, AK023227, AK021695, AF132856, AF068289, AL157877, AL137707, AL139008, AB040962, AC005993, AL157384, AL355916, AC004975, AL034379, AL158832, AC013429, U62317, AC005730, AK027217, AC020908, AC006536, AL138733, AP000048, AC005081, AC009032, AC004626, AC005821, AC005383, U91321, AC003048, AL109758, AL031274, AC005829, AF045555, AC008745, AL121997, AC003101, AC020913, Z84466, AC002477, AL132773, AL022316, AC010422, AL133174, AL118505,

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HODFG47	918	105996 9	1 - 1250	15 - 1264	BF345673, BE732149, BF684799, BE732105, BF973626, AL521968, AA922195, AW873081, BG249168, AW194609, BF310138, AW197591, BF341027, BE537520, AI185740, AW965809, BF694016, AI149726, AI800098, AA305846, BF341904, AA640513, AW675226, AA935807, BG117398, AA312842, BF341862, AA713593, AW449858, AA470048, BE876387, AA704143, BF110474, AI628310, AA176983, AA737820, AL521967, AA397353, AA702002, AA983700, AA975245, AA863436, AA983708, BF570805, AI471343, AA416876, AW965126, AI282285, AI913509, BE081596, AW376741, T32544, AW505291, AA046362, AW363086, AA724214, AI610316, R84594, AA714758, AI915421, N47199, BE081889, AI670874, AA442519, BE266231, AI954659, D19789, AA773604, BE264023, BE082127, AL538302, BF204069, AI479754, AI678909, F30845, BE774943, N28698, AF132856, AF068289, AL157877, AB040962, AL139008, and AL137707.
HBIPC05	919	106013 7	1 - 1003	15 - 1017	AL537138, AL537137, AI403115, BE464560, AI049667, AI921266, AI476756, and AI680380.
HOPJI32	920	106019 3	1 - 991	15 - 1005	BE559626, AA648932, AA742693, BF196375, AI243725, AI417050, BG107805, AA877170, AI400330, BG055356, AI688228, AI688239, AA682467, AA918714, AI033070, AA701935, AI250796, AW264399, AI243869, AA705038, AA743538, AA227787, AI735761, AI160787, AI807505, AI376819, AI078674, AW043673, N33011, AI247552, AA860111, W93664, AA284309, AW515896, AI351848, AA757540, AA677285, AA461254, AI417138, AA625139, BE908226, BF570801, AI765604, AW949994, AW949993, AA907925, AI219692, BF030135, AI699352, BG177209, AA731398, BE788620, AU122917, AA807487, AA723789, AI333471, AA946979, AA015678, AA767126, AW410993, AI198618, AW016005, AV720207, AI365028, AA975429, AA677912, AI167442, T95667, BF132906, AA918597, T27775, H49351,

						AI351115, AA017653, H59259, F35676, AA227786, BF912603, BF908138, BF571619, AI022007, R92112, BF196370, BF196376, BF795585, AI424112, AA856682, BF218248, AV763234, AV712432, F35677, AA372488, BF092387, AW381917, BF094621, BF217712, BF094671, AA374937, W93663, AW580421, AA345343, BF092528, AC004948, and L07493.
HNOBN20	921	106038	1 - 1545	15 - 1559		N47880, BF334493, AW469956, AW363838, and AC004671.
HOCPX74	922	106039 1	1 - 1870	15 - 1884		AL524597, AL519648, AL530831, AL519649, BE734258, BF347653, BE871077, BG104745, BF348323, BF343876, BG104449, BE869842, BE88412, BE273552, BE780351, AV690410, AW170543, BE314522, BF795175, BF663039, BF375780, BE149568, BF913222, AW603794, AW604899, AW001348, BE297766, BE265374, AI335452, AI925444, BG164669, AL524596, BF528067, BF975942, BE797960, AI608844, AL536780, AI817215, AV685897, BG029777, AI591352, BG178695, AI811673, AA853941, BE157959, AI805743, BG011563, AV729006, AA565014, AW604898, AW973191, AI345340, BG258971, BF445253, AA279139, BF352395, AI832033, AW604905, AI366971, AW152126, AA923303, AI366962, AI382206, AA434149, AI934699, AW362579, AI571300, BF330697, AW604908, AI628955, AI334950, AI201993, BE565222, BE275563, AV692860, AI913195, AW190506, AI553809, BE263940, BE263361, AA478024, AI766662, AI860471, AI435257, AV706788, AW274219, BE367651, BE267179, BE675074, AI340530, AA733167, AW073037, BF914370, AW609796, AA825666, R84539, AI581149, BF594915, AI949327, BF330696, AW104823, AI675988, AI393781, AI359747, AA292729, AW089578, AW301969, AV749661, AA434430, AA057489, AI628311, AI041758, BG058748, BF832690, AA485730, AA936549, AI969209, BF982895, AI377017, AI923566, C06478, BF887827, BF793586, AA459081, AA458890, AA564803, BE259264, BF887828, AI914921, W79182, AA057212, AI004361, W74428, AI349785, BF765630, AI687123, BF737458, AW966062, BE063151, AI359732, AI689065, AI167359, AI626037, AI34448, AA434203, AI288378, AA652404, AW956458, AI345581, AA293168, AI348864, AI349414, BF756936, AA740650, AA026165, AI343129, N95348, W25257, BE732289, AI376726, N68518, BE063152, W79074, AA810877, AV746022, AW071400, BF762446, AI312239, AI313347, BF895302, W00714, AI214147, AI457337, AI349751, R87384, AI018718, AA588542, T11665, AA953579, BF847574, AA310626, BF817632, AI085839, AW439522, AA429455, AA278412, AI042587, AA604993, AI434894, AA484907, AW272911, AA428689, AI254351, AI207020, BF829151, AA552581, AV696837, AA053182, AA580658, AI340724, AI349182, R85670, AW873126, AV657729, AI954961, AA573103, Z40757, AI090867, AI301832, BF876341, AI088716, AV696392, AV684547, R88960, AV745986, F34685, AW768933, BF346694, AI338123, AI811398, R89629, BE150220, BF829538, Z46084, AV749887, AA079521, AA434271, AA349776, BE089845, T32439, AI362261, AI571605, AI207037, AA079569, AA293308, T51217, AI907977, BF851263, BF526982, AI369567, AW576248, AW188668, BF894716, Z43547, AW973210, H27199, BE062964,

HTEPP27	923	106041 5	1 - 720	15 - 734	<p>AI682013, FI1048, BF686146, AL078621, AL137714, AK024481, AJ271736, Z84812, AF282037, AC008013, AC009533, AC008993, AK024448, AF327162, U12257, Z95360, T40837, T47278, T77603, T99381, R41279, R43475, R43475, R49647, H27200, AA015864, AA026214, AA053628, AA084023, AA084024, AA514350, AA291826, AA411542, AA482500, AA482648, AA486450, AA496538, AA707896, AA884801, AA934067, F02886, F13024, F10620, AI274729, AI343061, AI580732, AI628892, AI185529, AI190106, AI273550, AI683609, AI689651, AI830275, AI874028, AI915151, AW189652, AW439885, and AW662324.</p> <p>BE906519, BF590795, AW166407, AA425184, N75682, BE549827, AI990649, AV690903, AV749752, A1768535, AA504168, D45332, R20997, N51177, Z43298, AW969016, AW207406, AA156619, AI024330, R81435, BF798183, AI476407, AW628995, BF093913, AK026377, and AK079610.</p>
HL-YAJ79	924	106049 5	1 - 854	15 - 868	<p>BE877313, AV707414, BE877897, BE898244, AI207423, BE880171, BE879486, AV712023, BE874183, AV646609, BE877724, BE877360, AV713937, AV646653, BE876255, AV646649, AV646504, AV728530, AV725312, AV704989, AV706544, AV708364, AV710865, BE876145, AV707576, BE875452, AV704821, BE876209, BE879161, AV717895, BE876129, AV704136, AV710411, AI653760, AV728726, AV727727, AV646639, AV704410, AV705900, AV646554, AL037048, AV646616, AV702289, AA669077, BE876191, BE874129, AV704743, AV716924, BE881017, AI557254, AL048429, BE877534, AI065079, AI133420, AI133314, BE877089, BE873910, BE878189, BE878144, BE874933, BE875679, AI064797, AV646560, BE879920, BE879482, BE877490, BE881406, BE878843, BE873856, BE881677, AV704545, AV709377, AV716245, AV723801, BE876227, AV701103, BE880558, BE880965, BE880379, BE892986, AV715880, BE892997, BE881087, AV702097, BE880616, AV715527, BE881605, AI884494, BE879931, AV701289, AI133218, AA081407, AV723748, BE877550, BE875048, AI061660, AV654563, BE876526, AV691015, AV716518, AV693793, BE876857, AV693806, AV723085, AV702987, AV725077, BE875611, BE875017, BE879660, BE898249, BE880104, BE881578, AA886596, AW188463, AV686634, AV716707, BE874992, BE877148, AV725697, BE874412, AV721842, BE883115, BE868953, BE872765, BE869861, BE867046, BE868935, BE877853, BE876076, BE874887, AV757464, BE872576, BE867519, BE866703, BE874381, AV729458, BE870019, AI888487, BE867152, BE878535, BE876950, BE871969, AI064695, AV702362, BE877908, BE878111, BE873978, BE869555, BE867007, AL037870, AV703548, AV686024, AI459473, BE868476, AV706391, BE876777, BE876151, BE878325, BE879105, BE881405, BE874441, BE875672, BE876996, BE876184, BE881324, BE877404, BE872183, AV701547, BE878096, BE876772, BE892671, BE876933, BE880480, AA659265, AV724031, AA487595, BE895696, BE876529, BE893859, BE867946, BE873745, BE878628, BE877533, BE876273, BE874818, BE878625, BE875010, BE877218, AV715658, AA594949, BE880710, BE880906, BE875274, BE898642, BE869867, AV761230, AI924211, AV719659, AV724182,</p>

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HCOOQ11	925	106065 6	1 - 875	15 - 889	AW007037, AI884511, AA886989, AW193931, AI817713, AI249758, AA865294, AI951033, AI264240, BE613246, BF312076, AL038486, BG112904, BE744581, AI951027, AW577113, BG236451, AL519420, AW188640, BF312870, AA996176, AI991217, AU148172, BF344181, AA731851, AA741112, BE046060, AA527051, N53946, AI827285, BE868637, AL514001, BE670726, AA596053, N40254, AA579782, AU158854, AI078704, AA631758, AW959940, AA011629, AI275213, BE042693, AI435452, AA873027, AI206083, AI143622, AI811645, AA411414, AI887412, AA291435, AA808109, N23620, AA570435, AW845068, AA135399, AI066472, AW513124, AA682204, N35737, AI344485, BF514798, BF980552, T56288, AW662379, AA401883, AA156540, AA934515, N32127, AW338269, R83770, W63671, AA676312, R73855, AI056012, AI193778, H81756, W00608, AI569186, BE221170, AA411416, AW025247, BF851746, W61083, AA614043, AI888903, AA502388, AI628321, AA904082, AA506667, AA827494, AI002292, AA740494, AI061269, AI926417, BF946323, AA877480, AW519260, H82073, AA961238, Z41638, AI268112, N23619, BE407605, T52457, AI569627, AI597779, AA888216, AA996210, BE301554, BF197866, AI636718, AA230148, AA157698, AA045288, N68931, AI241476, AI520807, N30126, BE813412, AA290634, R02156, R66915, AA513443, AA513637, BF771899, BF982556, BE963002, R27899, R73856, AA007540, AA876184, F21046, R33645, BG115606, H77609, AW793338, AI589492, AA229874, BF990846, AA291041, AA502601, AI368907, T54493, F04593, AA807759, AW449509, R42729, BF206077, BE004381, BG122255, AW780372, BF512161, H84829, T54441, AI971366, T79762, R27807, AA078930, AA782709, AA228443, BF980481, AI538648, AA228276, AA011628, N24545, BE703483, BF835233, H85291, N33993, AA953353, AA135953, BF434060, AI371269, BF738422, N56794, AI940121, AA844546, ---, AA007539, R83623, AA345305, AI423659, AA886375, AA362021, AA360790, BE706771, AI368904, AI940130, AI345688, AW022682, AW161156, AL119828, AI521799, R36363, AW080402, BG033199, AI868204, AI567582, AW827289, AL079963, AI559632, BF525883, BF525838, AA287231, BF338002, BF885081, AI446538, AW673679, BF982265, AW834302, AL514879, BF061283, AI500061, BE785868, BF680131, AI440263, BE964614, AV723953, AW827206, BF968666, BE965621, BG164558, AV712672, AI249497, BG121959, BF856052,

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HWMGI51	926	106071 1	1 - 819	15 - 833	

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HDPJG33	927	106078 0	1 - 1156	15 - 1170		BF970702, AW167099, AI628843, AI093592, AA470016, AI926603, AV718913, BE670151, AI986035, AI027777, AI313500, AA782005, AW473593, AA412294, AI299627, AI610236, AA617710, AA514353, AA423925, AA860421, AW131013, AA781518, AA423887, AI1160307, AI446603, AW409605, H30472, AW169172, AA533814, AW368627, N69522, AA654163, AW513267, AA922534, AI440188, AI049694, AA412735, AI306695, AA865403, AW068125, W69267, AA459402, AI347601, R26875, W69345, AW959274, AA534481, BF810819, AI865836, AA745698, AI002434, N79834, AW044069, N58666, R72510, W67475, AA626929, AA932913, AL044134, AI539588, AL044135, R72511, AA430220, AI223230, R70436, AV695422, AI902383, R53036, H72504, AI383150, N54138, AW088334, AA545735, AI186385, AA359811, H24955, AI205760, BF946002, AA491113, AA024807, BE825978, AV744309, W38450, R94735, AA834248, N58200, BE242095, AI752781, R69450, BE543595, AA431234, AI648587, AI902360, AI436086, F04994, C17844, AA295920, AA552310, BF801989, AA034305, H77299, BF802042, D29280, H72902, AA861991, AV651047, AU154873, W67476, BF511557, R11021, AA411966, AI051263, BF914312, R27103, AI926118, BF855633, BF339384, R53035, AV651824, H25748, BG231151, AA432254, AA865593, AA643144, BF306192, R94818, AI016462, BG164558, R72498, AL042382, AL119399, AW983783, AW983832, BF970990, BG168696, AI538850, AI494201, AA225339, AI308032, AI344785, AI824576, AW074993, AV682479, AI312152, AI802542, AL079794, AW983829, BF904180, BF814357, AV743962, AL119457, AV741327, AI537677, AW075351, AI349614, AI698391, AW161156, AI349937, AI620075, AI829327, AI564749, AI885982, AW079572, BG113188, BF812960, AI270183, BE965129, AL046942, BF968910, AW162194, AI340603, AI478123, BF792961, BG029829, BG113299, AI610362, BF925729, AI345688, BF792928, BE544111, AI436456, BF885675, AI334884, AL042544, H89138, AI869367, BF725868, BG030364, AW148320, AI343112, AI624293, AI923989, AW051088, AI349598, AI349256, AW008085, AW129929, AV753074, AW263453, AI687415, AV759831, AI696846, AI440239, BE964614, AL048871, AW020693, AL036638, AI612913, AI696626, BF904265, AW950035, AI890507, BG249582, AL041772, BG256090, AI916419, BE895585, BE047852, AV681858, AI950892, AV738991, BG166654, BF680133, AI570807, AL514359, BE963838, AI623682, BG035511, BF061283, AW880037, AW050850, AI961589, BE966699, AI537273, BG257535, AW169653, AI345735, AI613038, AL119863, AI282281, AI591228, AV704051, AI802240, AL110306, AI798456, AI446538, AV760409, AA761557, BG179993, AV733470, AB046851, X52574, AK023297, I89947, Y11587, AF130055, AF119899, A65341, I48978, AJ006417, AK025092, AF017437, AL110280, AL162002, AL137480, AK026408, AK027096,



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 AA666029, AA719235, AA833627, Z19559, AA852192, T03659, A1005289, A1026024,  
 A1040304, A1093084, A1122568, F09128, T82315, T98040, AA693906, A1252237, A1269847,  
 A1289066, A1337191, A1350840, A1150959, A1623487, A191300, A191476, A1651710,

HOFNH33	932	106118 5	1 - 1957	15 - 1971	<p>AI652956, AI277935, AI286169, AI334059, AI335811, AI634317, AI609895, AI696221, AI744160, AI758994, AI865586, AI885755, AI887446, AI950152, AI933423, AW003340, AW082426, AW128882, AW292150, and AW473705.</p> <p>AA195087, AW957374, AI670093, AI669240, BF105071, AI151442, AW411125, AA425467, AA194946, W40431, AI808052, BF204013, BF732418, AA700297, AI078393, AI688673, AA024998, AI671406, BE502303, BF512887, AW411124, AA702853, H12618, AI189137, AA195556, AW966185, AA425375, AI656096, AI287581, AW195085, AW885572, AI800331, N93931, T33450, AA195752, AA195715, R66048, R66047, AI654892, H12668, T33449, BF057001, H90799, AU117292, H02011, AA115390, Z44587, T35437, T29924, AA337449, AA133417, R24216, AI300252, AA024872, AW885729, AA336400, N98972, AA903701, N69833, T20253, W90007, R24215, Z40465, BF059554, AA373336, H90748, AI473272, AU144172, AC023154, AK021492, and AX013081.</p>
HAAJAQ63	933	106123 8	1 - 3970	15 - 3984	<p>AL515424, AU133217, AU117140, AU142384, BG033833, BE876803, AU139465, BG259851, BG167796, BE743306, AW473531, AU135959, BE875637, BE888606, BG260336, AW580231, BG107108, BG179511, BE887292, AU233825, BG027450, BF671771, AU119885, BF575632, BG036892, BF791887, AU117158, AI689392, AI969513, AU136366, AV752386, AU127278, BF794737, AA577695, BF347777, BE539387, BE888461, BF035474, AL046713, BG107285, AU135160, BG025131, AL039354, BF061987, BF812543, BG031453, BE734936, BF212314, BG259074, BF981318, AW851018, AW957785, BE552121, BF819996, AW379372, BE835355, AL039548, BE893099, BG032762, BF693254, BE439886, BF209896, AL040257, BF207817, BF688672, BE466166, AW965646, AU138546, BE888383, BF514065, AW814786, BE889498, AU144064, AI338724, BF528934, BE568710, BF790899, BF790348, BE969916, AU151881, BF381749, AI753682, BE537675, BF038173, AA927334, BF240276, AW966689, BF242051, BE835432, AI742904, N20178, BF103706, AW963156, BF382259, BE567450, AW369137, BF750387, BE280960, BF920929, AA313265, AA196578, BF744444, BF693176, BE961188, BF814166, AL048800, BF669614, BF695646, BF747979, BF573281, AA584433, AW205552, BF210307, BF930968, BE967604, AV758139, AW075512, BF229128, AL041181, BF931659, BG014272, AW957862, AW297463, BG032249, BF696371, BF242624, BE841199, BF904837, AW293263, BE537740, R70619, BF789995, BE889296, BF247682, BF934769, AW814722, AW517759, AA076256, BF688897, AW369831, AI580344, BF965679, AI917185, AI348555, BE089815, BF742017, AA579344, BF930639, AA578603, N29079, - BF750787, AA747403, AA649704, R80337, BF102774, BF674705, AV747890, BF210080, AA355742, AI281795, AA326479, BF028979, H11175, AA083989, D82206, D82173, AA642754, AA326164, AI515423, BF229913, BF238375, AA363512, BF672447, BF977594, AW075837, BE736387, BF742025, AW576881, BF692010, BF820629, AA344537, BE818113, BE001659, D82200, R60858, AV738050, AA650232, AA808866, BF375716, BE972715, BE893554, BE818095, BE172915, R22704, AU077250, AA133820, R13289, AA301326.</p>

					<p>N57164, BG255786, BF212867, AL046786, BF348022, BE088453, BF693404, AA092609, H06323, H87922, AA654758, W26917, BE167529, BF215056, BE895957, AA167156, BF901255, AW821022, T05303, BE813024, H93588, AA363584, AI928366, H05331, D58857, BF245942, BE081882, BG235926, BF692607, AA360920, R66345, F07286, BE172376, BE818048, BE818060, R81874, BE896503, BE936475, AW607901, AA454112, AW999261, BE936455, AW383272, C16797, N88563, BG110805, AL119107, BE818043, BF031668, AW074610, AA384710, D53920, AB018266, AK001388, M63485, AX014885, AF117236, M63483, AY007157, AB009275, AB009276, AB009277, AL159986, AJ224169, AJ224166, AX030435, AC024094, AX030436, Y17793, AL117541, AF064854, AF019249, AL133053, AL122101, AL133049, AR071207, AL133074, AL133076, T94600, R66804, W56842, N85026, W28960, N86432, N87313, AA093822, and AA095354.</p>
HVVVK70	934	106125 8	1 - 1629	15 - 1643	<p>BE746661, BG117435, BG252083, BE877320, AI806227, AA178948, AI016759, AI653545, AW573210, AA927605, AA631986, AW592037, AA531275, AI018243, AI660515, AI831705, AA568173, AI984148, AI581183, N98668, BE379164, BE271705, BE746583, BE394807, BE272756, W88624, BE887776, BE393523, AA004850, AA134872, N94263, AA426075, AA045761, BF435518, AW376913, AI673780, AA719164, AI345684, BE047692, AI921655, F36014, N69655, W88625, AW370783, AA004659, AL040320, BE882506, AI199851, AA045760, AW378878, AI682887, BE062798, AW370763, BE297968, AA634581, F32535, AA583661, AA025749, H13681, AA405861, R97397, AA134873, BE296854, AA046099, BE733701, AI829163, D58431, BE743785, AI863398, F24760, AW009286, AI440272, AW885403, AI940469, BF590167, AI688326, AW935165, Z24923, F22372, BF742972, BE879452, F33891, BF826768, BF856608, AA045994, BE621382, BE733458, AI832776, AI357679, AA043984, F19411, BF856598, BF857638, BE311732, H13728, R97441, BF856594, R24161, N66145, BF856596, R49671, BF856586, BF856597, AW601232, F36904, AA025901, BF826760, BE407674, BE278843, R24175, H01735, BF857636, AW379124, AW379128, H00992, AW104282, T61947, AW379135, BE730674, BF105945, BF087158, Z24932, AW601233, AI640673, AA044038, F35309, BE538525, AW379126, BG118318, AW362195, BF835188, AV706662, AA128148, T59326, AW379134, AA178993, AW853877, AW378910, BF857639, BG111319, AA618396, R26642, AW850722, BF510012, AI690017, F31129, AW850563, AI689995, BE301917, F30217, AW379136, AW418766, AW378905, F34755, F22842, F00363, AA345998, BG013553, BE065767, AA034504, AW805008, AA936926, BF773367, AW804639, AI656281, BE965287, AI868108, BE277985, AW372049, AA126983, AW381206, BF351128, T62177, F37877, BF810848, AI905007, BF857640, BF773378, AA223532, AA223444, BE618269, C18341, BF914199, AJ000414, AC008760, AC020954, AB006914, L40379, AR032003, and F22843.</p>
HVVBA82	935	106133 2	1 - 946	15 - 960	<p>AV758998, AW104667, BG111699, BF984753, BF981305, BG036253, AI660239, BG181014, AW192662, BF981880, BE549196, BE541171, AV734020, BE220777, BE748099, BE538578,</p>



					BE675535, BG034157, BE743707, BE781960, BF348443, AV761028, BF679820, AA149387, AW675599, BF978927, BF215587, AW515451, BF032015, BF670435, AA847574, BE857449, BE77637, BF132730, AI539738, BF239050, AA135732, BE748644, BG168280, BF211380, AI300901, AI268828, AA22637, AA531567, AI357994, AI309050, BF836098, N20619, AV763501, AA936062, AV711600, AW672918, N93282, BF810979, BF690985, BG056323, H49133, AA422000, AA425729, AW044436, AI740706, AI539737, AA931709, BF696241, N41898, BE972524, AW515413, AI017377, T83643, AA424838, BE879189, AW406931, AA135776, AI523674, AA422076, H62744, AA512991, W25122, AA374578, AV707541, AV721902, H20901, AA335669, T81252, R65722, R68402, R01195, D80535, T75066, AA331147, T55701, AA360427, AA151477, R16704, AI369338, T83806, D80859, W23283, T55617, D60042, BE707866, AW673282, H69272, AW074460, AW385013, AA331146, AW263458, R10838, R97305, AA349005, AA336200, AI214651, AA354131, AW665284, AA335103, AA335929, N88208, AA373357, R68603, D81732, BF773431, BF570530, BF090530, BE165563, BF757003, BF929244, AA418654, AA424305, AW675634, AW473911, AA401527, H98948, BG169743, AA418592, AW860841, BE165439, AI741767, AI263917, N32554, BE165564, AA338792, AW802151, AA365792, AW953995, BF347938, AI336124, AI831187, AL022313, U78678, AF276920, AR052467, A89699, D87741, U85089, A89697, U73525, A89724, A89726, and A89725.
HWLLG38	936	106138	1 - 3477	15 - 3491	AI096614, BF689518, BF689602, BF690438, BF690510, BF316501, BE858130, AW340728, AI810241, AW963861, AW149761, BF439069, AA903390, AW953324, AV728578, AV651868, AA977686, BF115903, AA581377, AI679552, AI91083, AW193559, AA593747, BF951855, BF951834, BF951868, BF951837, BF951879, AA978316, AI827255, BF951847, BF951864, BF951811, AA706200, AA457517, AA004873, N48605, AA351076, AA005076, BF951809, AA457611, AA780194, BF951839, BF951873, BF951861, R53320, AI933315, BF951820, AW591270, T03623, AI348123, AA856593, W79233, BF951887, BF951804, AI014427, W69950, BF836260, BF951858, AV708382, AA777076, AI457647, AW512874, AA351330, N49195, W69951, BF951791, T74434, BE328207, H22041, AI679992, BF951822, T33676, T09286, H18390, AA780327, AI017000, AA514385, W73991, AI344364, H28035, H20510, M78434, H17240, T23476, H40171, H20600, H84107, R98653, AI566944, AV697649, T35667, AL524444, AL521769, AI358855, H84108, AA909477, T15763, AA376577, T78763, AI950107, R38753, AI038515, AW804533, BF834235, AL520806, AI423916, H40102, AW472773, AW900772, AV686990, T34809, H18389, AI272344, BE858146, T80029, T33765, AA827327, BF951794, BF810830, BF951803, N69080, BF812152, BE783055, AI873905, AW391924, H52821, AV728984, R52662, R46036, BF853739, AA336464, AA320503, BF952167, T33307, T16116, N47288, R61643, AW800900, D52198, F02316, AW992840, BF951890, AA324827, AA688361, AA725715, AI873019, H39520, AW894762, N53892, AA365710, AA629117, T07134, BE076511, AW869238, BF091468, AW203994, BG014481,

HTPCH84	937	106146 6	1 - 1210	15 - 1224	AW385119, BG014470, AW993215, AI014291, BF155426, BF952168, AA569810, AP000426, AF052142, DI0884, DI6227, AK000596, DI13126, AC007249, AF070616, AP001329, and AF131813. BF339551, BE878006, AW083241, AW262121, BE878908, BE873766, AW662363, AW471440, BF001490, AI718743, AW083914, BE879166, AW014771, AI857725, AI290210, AA025673, AI520716, AW769220, AW006931, AW204999, BF591174, AI561219, AI380034, AW080544, AA613366, AW771720, AI282851, AI185297, AI624643, AW272130, AA740147, AW083605, W67560, AW801019, AW316995, BE877829, AA603704, AA577603, AI910466, AA514270, AA158406, AA155646, AI446656, AW080904, M91489, AW955349, AI472456, AI862475, AA025672, AA325843, AA155701, AA639402, BG251426, AI791349, AI6233302, BE879306, AI432644, AI431337, AI432647, AI431307, AI431316, AI431346, AW972093, AW968355, AI432675, AW968356, AW968729, AW972092, AI432674, AI432676, BF859009, BE672745, AI431347, AI432653, AI431230, AI431328, AI432654, AI431354, AI432655, AI431310, AI431312, AW081103, AI432650, AI432677, AI432661, AI492519, AI431330, AW128897, AI432649, AW971740, AI432651, BE672748, BF448552, AI431238, AI431248, AI432643, BE672767, BE672759, AI431345, AW972090, BE672743, BE672719, AI431353, BE672742, AI432658, AI492510, AI432672, AI431243, AI432666, AI432665, AI432657, AW972091, AI431247, BF589777, BE672774, AI432662, AI431357, AW128900, BE672625, AI431351, AI431254, AI431241, AI431255, AI432673, BE672644, BE672732, AI492520, AI431751, AI492509, AW129223, BE672738, AI431231, AI431257, BE672792, AW969229, AI431308, AW128846, BF589864, AI432664, AI431350, AI431323, AI431318, BE672626, AW079749, AI432645, AI431235, AI431321, AI431315, AI431314, AW128884, AI431246, BE672749, BE672744, AX017828, AF104419, AL157435, AF217794, AB029011, AF217793, AF134240, AL121845, AF217796, AX030436, Y17793, AX030435, AR071207, AF064854, and AF019249. AU133671, AU135250, BE886299, AW364014, AW364012, AW364015, BF789904, AW364019, AI760785, BF381648, AI384093, BF691155, BE349308, AU155185, BF665614, AW628405, AU157168, AI224905, BF210459, BE565115, AA282933, BF086868, AI267509, BF573653, BF696297, AA513728, AA729606, R80458, N76465, BF573488, N59362, AA334630, AA300682, BF211785, R69849, R80659, AA573139, AW614666, H86676, AA427982, BF106221, AI499874, R31977, AU152566, AI351352, AU154907, D61921, BE885576, AW471080, AI091339, AA310325, AI051323, AA830587, AU134074, N67319, AU155924, AU152872, AA449856, Z99396, AW877209, AA621436, BF868687, AW979204, AW975002, AW975037, AW975028, AW975965, AL119324, AW975031, AW972292, AW976024, AW975032, AU143049, AW604723, AW974374, AW392670, AW974089, AL119457, AW974801, AW971254, AW979127, AW972377, AW979212, BE705905, AW975433, N93060, AW969803, AW858526, BF436338, AW134482, BF868684, AW979288,
HWLHJ68	938	106152 1	1 - 1662	15 - 1676	

					<p>AW972845, AW969885, AW972373, AW973270, AW970113, AW975004, AW974663, AW972884, AW973202, AW972695, AW973805, AW973213, AW972719, AW971375, AW976515, AW975976, AW971387, AW979165, AW973770, AW976510, AW971954, AW972680, AW975975, AW969884, AW972943, AW969759, AW979083, BF592735, AW976982, AW970587, AW975876, AW973650, AW979175, AW973986, AW979064, AW975938, AW975016, AW975138, AW975966, AW975968, AW970921, AW969766, AW979116, AW972806, AW973987, AW975910, AW975943, AW972689, AW972706, AW973164, AW970097, AW973824, AW971964, BF588769, AW975904, AW974379, AW969752, AW976037, AW973718, AW973967, AW975933, AW979169, AW973207, AW979176, AW972882, AW973104, AW969782, AW970868, AW972868, AW973985, AW973210, AW975648, AW971129, AW971403, AW973209, AW975971, AW973185, AW969930, AW972864, AW973219, AW969658, AW972440, AW979178, AW972883, AW979081, AW972933, AW973167, AW975162, AW972637, AW973750, AW971183, AW970110, AW972705, AW972827, AW973946, AW976012, AW979147, AW972823, AW970589, AW971259, AW971350, AW975261, AW971367, AW972685, AW972690, AW972817, AW979294, AW972371, AW975229, AW970978, AW971968, AW972880, AW979085, AW979228, AW972699, AW979220, AW973190, AW974915, AW973088, AW975173, AW975955, AW974107, AW971429, AW969861, AW979219, AL036418, AW972808, AW973728, AW979210, AW969839, AW972212, AW972866, AW972417, AW973271, AW975018, AW975928, AW979201, AW972837, AW975964, AW972816, AW979090, AW969753, AW973997, AW975106, AW975168, AW975025, AW971415, AW972711, AW972889, AW973804, AW971414, AW971413, AW975914, AW975922, AW972710, AW973740, AW975172, AB033047, AK023596, AK001587, AL136109, AR066494, AX046357, AR060234, AJ279014, A81671, AK024026, AR023813, AR069079, AR064707, AX030435, AJ251859, AB026436, AR096545, and AR054110.</p> <p>AU120416, BE744242, AI802087, AI334107, AI679782, AA668147, AA77986, AI610074, F24745, AW814632, AI065031, AA904211, AV762162, BF984148, AW754413, AW754426, AU146342, AA482928, AI791659, AA584151, AW023111, BF991881, AI031759, AV758870, H68343, AI818362, AA873176, AA577748, AW237905, AA525331, AV720457, AW151247, AA584655, H85808, BF763954, BF991882, AV760014, AA558404, AL042667, AL042670, AU147414, AW572721, AI859834, AV761107, AV732057, BE243207, AW471332, AI452836, AW243817, BE090515, AI669421, BE154832, AW275432, AW151761, AW976024, T74524, AW754429, AA297776, AI355246, AI499954, BE138594, W96522, AV730440, AA425924, AI187148, AI251429, AL037910, BF725844, AA633875, BG054730, AI755214, AW576251, AW192599, AI569100, AI754567, AV763026, AV763058, AI038304, AW117860, AI049955, AI457313, AV756491, AI634187, AI446336, AW962611, AW500684, AW674631, AI249688, AW069227, BG026977, AA489390, T47138, AA666295, AA644090, BE396138, AW958962.</p>
HLGDA34	939	106154 3	1 - 1756	15 - 1770	

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HAICB08	940	106162 9	1 - 418	15 - 432	BE548483, BG011743, T83015, C18279, AA143436, BF149348, BE737483, AA625504, BG015853, EI6696, AR060023, X84325, and D89821.
HVVAW60	941	106169 4	1 - 1751	15 - 1765	AL522960, AV716079, BE562316, BG257743, BE514489, BE514402, AW960737, BG118714, BF305711, AV760248, BG168581, BE908798, AI676130, BE396634, BE296285, BE548005, BE883381, BF027184, BF184561, BE564819, BE295446, BF210212, BE786704, AV728718, BE549142, BG113812, BE565708, AI991800, BE379623, BE537293, BE269782, BF031906, BF732339, AA307685, BE019417, BE589492, AI936232, W67860, BF541439, AI640485, AW573248, BF184405, BF002320, BF196840, BF305465, BF211313, AI628790, AA524353, BE380048, BE270486, AI824956, AW590315, AI990762, AI800990, AI335005, N31143, BF110487, BE568262, N21294, AW152627, AW612791, BF976876, BE565937, AW302169, BE268289, AW002644, N21128, AI333331, BF594576, BE671185, BE565017, AA994852, AA983846, BF571446, AA595031, AI420382, BE208007, BF241220, AW801675, AA610108, N90992, AW071591, AI240604, BE464059, AA678009, N31229, AI264921, AI655233, AI611678, AW819529, R70013, AW819596, AW749326, T64746, T31944, BG112244, AW015641, AA084445, AA579237, AA570191, AA935035, C15927, AA358195, AA081627, T07826, N94623, T34036, Z44938, AA380035, AW819534, BE961033, AA579517, R58098, BF593322, Z44410, N69498, D60023, D52558, AW373952, AW369584, R70058, AW732725, BF377913, BF155961, AW373174, BF088421, BF831228, AW373195, AW089404, W23822, BF377935, Z41687, BF831227, BF093517, T83793, BF088432, T32675, W67803, AI566308, H98950, F03903, AA358196, AI360228, AA913439, AA094862, AA129262, AA129234, BF734127, AK026636, Z85996, AF151882, AC011742, D16898, and AF090992.
HPDVVB50	942	106170 8	1 - 2277	15 - 2291	BG110784, AU133851, BE895171, AU139859, AU136530, BG252145, BG110641, BG030216, BG115009, AW885996, AL522229, AI750569, BG180358, BF665151, BF701424, BG250200, BE622539, AW953720, BE879873, AU136623, BG163703, BE746945, H98997, BF668726, AI453574, N45209, AI038373, AV715925, AW157069, AA488398, AI031961, AI936414, BG055400, AU157578, AA917614, AW613506, AI242693, AI830692, AI817023, BF575831, AA975353, AW873961, AI379087, AI393586, AI969695, AA706024, AI469100, BF726482, AI143014, AW163037, AW029292, AA873241, AI375856, AW068933, N75082, W47315, AI206378, AI131506, AA868954, W37909, BF031608, N47942, AW194555, N40179, AI857755, AI521640, AA195724, BG118437, AA147923, AU156272, AA031314, AW055122, AL523048, BE175623, BE175622, AW197580, AA931438, AA195737, N20825, AI630350, AA534465, BE622705, AA635980, AA027826, AI347838, AA456304, AI041938, AI359317, AI671889, N53037, AA488531, BF209307, AW967825, W61353, W37969, AI042257, AI039277, AI266252, AA243394, AU157831, AA456702, W96493, AI184272, AI862590, AA583907, BF030909, BE045250, N26004, N59632, AA582503, AA632122, N27670, BF214953, AI651899, AA670437, BF195792, AA581612, W07653, AV653088, AA836144, AI825487, AI128759, BE465673, AA291904, W47200, AI183354, AI800321, H45131,

	943	106176 5	1 - 3107	15 - 3121	<p>AI301659, HI7346, AI276999, W20055, AA252488, H83333, AA724930, AI250811, AA625971, AI452718, AI341898, N29709, BF668882, AL525861, T30345, AI621193, T34303, BF669704, AA992663, AA836760, AA047567, AI864958, AI891142, H02501, AI266031, H72719, BE738881, AA491989, AA291166, AI356738, AA630028, H26432, AA962161, W03223, H72718, AI566181, H13511, AI094636, AU138354, AV645409, H02502, N66130, R97194, N52312, BE004459, BE966654, AA876250, H55843, H63580, AI159829, H78295, AI334377, Z32891, BE165958, H78296, R63440, AA932971, N58559, AV689157, R63386, H26909, AI351585, AA885854, H83691, AA577175, H45434, BE873203, H55752, AA481154, AI039244, R76721, Z45752, AA976447, AA782746, AI208353, R76382, H26283, N91454, R64107, R31472, W25669, R31473, R33124, AA156043, R64198, AI474436, T81765, BE618282, BF696773, AA884149, AI498792, N98653, AA732532, AA890647, AV646901, N69563, BF358942, T90839, AA156020, AA354336, AA443805, T34995, R30936, T82078, T85747, AI208477, H63538, AA723952, H89847, AV695034, H47823, AA992834, H27713, AI523027, W69225, AA031423, Z38434, T49868, R33276, N94054, AW444875, AW176679, AI002030, AX014900, AX040014, AX040013, R23720, R23767, R28666, R33241, R82873, HI13454, H90694, N73221, N78162, N78185, W96367, AA027887, AA195701, AA470628, AA586507, AI000517, AA095675, AA664112, AA777160, Z41404, AI128982, AI200005, AI659761, AI522073, AI685009, and AW299491.</p>
HAZAY40	943	106176 5	1 - 3107	15 - 3121	<p>AUI24207, AA878323, AV727477, AA813018, BE819431, BE819398, AI982712, AA633959, AW950933, AI956077, BF064281, BF109192, BE140132, AI208234, AV727935, AW383147, BE219365, AV728174, AV728496, BF338980, AA778801, AV727596, BE677722, AI474131, AA918211, BG250843, AI458506, AV706403, BF761352, AW196922, AL046869, AI199333, AV726144, AI754255, AW189937, AA101251, BE140101, AW008386, AA629410, AI276190, AA729919, AUI137006, AW383099, AA411867, AW379346, AA411868, AI122819, AL046278, BG112787, AA350955, AL043466, AA778905, AI129808, AA906089, AI092120, BE938096, AA909370, BE220435, AW950111, AU156976, AW956564, AI217746, AW957591, BF093718, AA724295, R59145, AA142828, AI150676, AI859223, AW629051, AA350954, BE003474, T28874, AW856987, AI372582, AV654911, AI891046, R79559, BF766005, D58168, AI372585, W86981, AA688237, AW630587, AA112699, AA634462, AL048948, BE843792, R52701, F03219, T78821, BF447006, AA332608, AA025541, BE007851, AW072205, BF960536, AW627416, BE818041, R52752, H05997, BE003009, AA025613, AI204948, AA386124, BE719764, BF924561, BF755685, D51900, H05950, R59146, F21451, R41764, AI372584, AA334615, AW992555, AL039813, BF913530, F13339, T03639, F06952, BE813304, AA350943, BF986036, D56855, R79560, AW379200, AA112698, AI372583, T57699, R77478, R14949, BE938524, BE844105, BE844110, R23531, R45204, T57740, BG260187, AW082382, BE707402, R44663, BF914630, BF515358, F05976, BF753509, F02220, BF750798, BF761340, AA368172, BF761346, R77577, BF929007,</p>

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HACMZ51	944	106176 6	1 - 5344	15 - 5358	BF795041, BG176854, BE889259, AI123797, AW968653, W80418, BG107937, BF978869, BG180159, AW967830, AI935417, AI741992, N21026, BF516218, AI435856, AA488922, AW967828, AW968651, BF514662, BE175744, BE296548, AA725895, BF515826, BF132005, AI743694, AI248795, AA682214, N53932, AI160081, BE175743, BF940732, AA806186, AA808294, AA581874, BF825333, W88973, AI057447, BG112400, AI240596, AI804003, BF439423, AA705427, W79026, AA194938, AA262401, AA485223, N54336, AA701482, AI192835, BE882217, AW977587, BE175765, AA459487, AA487727, AA258332, AA410401, AA195537, AI089098, AA253015, BF672536, AA700235, AA258496, BE931749, R70964, AA742366, AA634985, AW968652, AA406446, AA972891, AA280738, AW967829, AI417670, H61661, N32280, W88972, AA243614, AA612844, AA809932, AI753396, AA676538, R96589, AA488851, W78956, D81704, AA578562, AI937703, AV750774, R91659, AA243594, BE218227, BF592077, BF431663, BF107149, AI350939, AI240751, R96590, W80450, AA599959, H59035, BG223302, N68753, H60057, N91646, N24728, AA253027, BF531077, AW182249, AA262626, AW449085, AA665027, H59401, N36709, AW572357, AA484946, N20616, N44566, BE465244, AA419347, AA034295, D60390, AW770441, AA748357, BF086114, H59036, BE172157, AV727020, D60753, D29339, AA279489, AW973702, H58990, R66624, H78860, N22621, AL135138, D80043, AB037744, T50378, T51069, T87331, T87432, T80282, R16493, R16793, R16889, R16943, R20740, R22221, R22276, R27597, R27696, R34517, R36581, R36582, R39968, R43467, R49072, R49692, R52816, R52851, R49072, R43467, R43494, R20740, R46644, R39968, R49692, R62955, R63008, R66425, R66819, R67917, H21718, H27063, H30186, H42692, H39131, H43926, H44586, H46389, R99312, R99404, H64752, H64751, H84964, H97190, H64752, H97608, N26236, N28697, N33047, N33556, N41538, N42109, N70229, N79806, N98255, W01018, W19986, W44335, W44449, W81010, W81009, W90684, W90779, W99356, W99386, N90413, AA009837, AA010386, AA010322, AA019377, AA019378, AA026243, AA029623, AA033587, AA033588, AA056089, AA056148, AA079689, AA081447, AA081752, AA082528, AA084728, AA100074, AA100159, AA113183, AA127588, AA134510, AA156575, AA157284, AA161199, AA161200, AA181973, AA187561, AA226873, AA226833, AA233473, AA234238, AA235690, AA256297, AA256403, AA417901, AA418057, AA430035, AA430244, AA492600, AA279831, AA468684, AA506011, AA506624, AA514562, AA587048, AA595566, AA604178, AA631096, AA573619, AA575906, AA579642, AA565772, AA714575, AA730078, AA742696, AA765252, AA812238, AA826845, AA904238, AA918044, AA922424, AA923043,

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HUXAL63	945	106179 0	1 - 3891	15 - 3905	U69567, AI125532, BF968973, BE890521, AF074692, BF968403, AW977280, BF111890, AV645725, BF797236, AW274041, BF002861, BF917447, AA434064, BG117266, AI559516, AU128956, AI569610, AV758189, BE047096, AW968976, BE044110, AW364486, BE842833, BF724803, AI041022, AW977686, AW188085, AW778740, AW471208, BF965471, AA058906, AW264922, AW936511, AA610288, BF102704, AI830921, AV750725, AI024731, W95811, BE885355, AI467943, W95857, AW474117, AA714833, AI332805, BF917665, W94729, W95818, AW276321, AA843441, AW473231, BF692464, AA725577, AI469526, AW301225, AI566211, AI376892, AI670697, AA827170, BF515424, AA043864, AW268885, AU157913, BF222606, AW304442, AW081224, AU139180, AW675227, AA936393, AI638422, N20661, AI632592, AI918739, AI446174, R70621, AW317070, BE148662, AW149140, AW592514, AI341172, BE045468, AI962441, AW580433, AW104291, AI963798, AA976362, AA627267, AW044184, AA884211, AA076173, AI687963, AW974151, AA927329, AW674700, N43830, AA489203, AI675470, AA706073, AA554058, AA043863, BE619745, D45459, AA128632, BF109435, BF198102, AA582316, AI689250, BG001662, AA075669, H88856, H05903, BF083956, AA960842, AW022044, H13597, H27633, AV682275, AA905245, AA588884, BF808593, F08282, F07961, F07955, AW028213, Z41033, D63110, AW196550, AA732684, AA055815, AA757169, AA504225, F04206, AW020016, T72574, AI364772, AV657834, AW385164, H88860, AA434339, BF083367, H88855,



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HLCLX57	946	106188 6	1 - 2115	15 - 2129	<p>AW949360, AW316853, AW089870, AA424629, AI201957, AI694683, AI042413, AI208793, AA424584, AW468856, AW243593, AI689654, AI887451, AI078571, W47195, AI348627, BE180539, AI868956, AI685858, AA242894, W52204, BE710410, R72819, AW338772, BF944058, AI871541, AA304463, AI284275, BF851275, AA593283, AA897431, R73270, AA579833, AA852334, AA853717, H43839, BE711428, BE695310, W47310, AW025730, AA298143, C01723, BE167889, AA834168, AI307300, BE836337, BF990841, BE766647, BF964609, BG009975, AW983550, AA382523, S82451, AC005479, Z37976, AF004874, U33363, and Y12760.</p>
HMALF63	947	106193 5	1 - 1152	15 - 1166	<p>AI373162, AL514198, BE744468, BE315169, AI879055, BG259216, AL534521, AL538110, BE548233, BE292875, AL535782, AL537844, AL519121, BG257178, BE895302, BE742053, BG169655, BG171616, BE790421, AI929358, AL531286, AL536936, AL517674, BE292962, BF725367, BF036696, BE622359, BE888207, AL537997, AL516034, BE889487, BE783803, BE882945, BG256087, BE889516, AW160574, BG165025, BF796758, BE784053, BE884321, BG177421, BE782424, BE873426, BE869356, BE885292, BE962078, AL037933, AL535845, BE879051, AI972935, BF306804, BE890568, BE882612, AU119653, BG168428, BE694068, BE783985, BG256542, AL048676, AL514830, AU128858, BF979567, BG179671, AW630116, AL048687, AU143723, AW003255, BG260833, BE939927, AW997244, BE787270, W20127, AA494315, AI734206, AA314388, AW954925, BE834065, AW401695, AA100745, BE782385, AA227875, AW402291, BG105799, AI188082, AI124658, BE870935, AW161447, AA485855, BE620451, AA071213, N24322, AW006363, H17687, BE244817, AA687282, BE867557, BE879392, BG008774, AW470363, BE501063, BE538463, BE895265, BG006671, AI815719, H29212, AW407681, AA100530, AA830489, BF949434, BE618384, AW339931, R59748, AA830488, AA113090, R56388, AA171458, AV653142, AA718924, BF949844, BF949846, D82199, AA351640, BF822910, D82234, BG010445, AW872599, R23526, AA218685, BE896855, AA316126, H23018, R25573, AA219744, T27125, T66781, T80306, BF088864, H06138, R59636, BE244031, BF752472, AW872480, BE243908, AA352235, BG180676, BF949926, T65622, R56750, BE831546, F07306, AA316123, AA676374, AA609598, BF981271, W22104, AA769956, R19429, AW407586, AA332399, AA905754, R18170, BE872713, BE242892, BE814852, BF752477, BE780714, AA465039, AA307240, AA884536, AI969327, BE865926, R14049, AA137233, AA366276, AA360745, H05673, H06931, F11952,</p>

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HACMR36	948	106205 7	1 - 2216	15 - 2230	AL514907, AL513615, BE790591, BE559884, BE793937, BE396311, BF314808, AU120211, BE871655, BF315412, BE312810, BG111263, BG249137, BG254548, BE783949, AW246222, BE253150, BE256829, BF196899, BE615313, BE615793, AV645348, AW249053, BE222572, AA582193, AI971522, AA633897, BE265100, BF062548, AW083860, AI146327, AI923961, AW027697, AW027689, AI679784, AI677984, BE223086, BE262799, AI860723, AW297187, AI553876, BF516242, AI524021, BF115386, BE205840, AI239829, AI677764, AA85076, BF588747, AI027576, AU144604, BF085665, AI811635, AA553825, AI971727, AI983956, AA211483, BF058201, AA599596, AI951110, BE266771, AA702849, AW166239, AA580220, AW248614, AI684649, BF941696, BE301721, AW169464, AA665482, AW304841, AW245146, AI004172, AW057556, BF108684, AA599674, AI672124, BF752889, R87478, AA216758, BF970240, AI204291, AI923433, BE926533, AI537686, R75912, AW732114, AI924338, AI291360, D31223, AA503759, AI394349, BG055744, AA317891, AA687790, H20155, BE255535, AI827071, BG057020, AI623743, BE645436, H64647, BF304487, H20249, H40207, AW503800, AU117909, BF205435, BF989017, BF997845, BF995585, BF204566, BF997846, BF989221, BF896934, BF995656, BF995504, BF995552, AW627631, AA776382, AI094448, AI919375, AA504325, BE298522, BE873199, BF346937, C14511, BF308581, H52717, AA917674, AI378986, BG029770, BE278600, AI696139, H52696, BG026227, BF725769, N40190, C14461, BF335338, AI559638, BF081784, C14410, BF981357, AI337287, D59458, H41559, BE857280, AI652150, AA553899, T12190, BF995508, AW005259, H40206, AA935183, AA585292, BF304742, AA664469, BF750859, BG222453, AW518325, H13363, AW074730, AI022018, AI908692, AW839602, AW628252, BF306336, AW839596, H30707, AA372402, C14497, AU128889, BE796866, H52973, AU123548, AA356031, AA809845, AU128801, D59779, AA218550, R88152, BG253048, BE548430, BF988348, AI924407, BG030548, BG259362, BF526001, BG122005, BG164994, BF971016, BG027631, BG250744, AI620284, BG252351, BF969798, BG027221, BG105848, BG259612, BG117545, BG108375, BG164495, BF793872, BF980532, BG166291, BF342312, BF344164, BF525514, BG259435, BG260963, BG028019, BG167415, BG179486, BG036520, BG169823, BG179183, BG170847, BG250790, BG105758, BF796661, BG178197, BG255566, BG248893, BG163974, BF347154, BG257498, BG167013, BF981953, BF793646, BG255388, BG256106, BF968284, BG167641, BF343702, AK001184, and AK000963.
HAOSM08	949	106207 9	1 - 2962	15 - 2976	AU125561, AU132527, BG252975, BF223038, AW960784, BG251220, BG120207, AI631712, AW003882, BF791715, BG117870, BG253108, BG029037, BG121891, BG252002, BE873094,

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HTEFM89	950	106208 4	1 - 2874	15 - 2888	AL519991, AL534720, AL519990, AU137078, AL037563, BE887697, BE889066, BE882061, BE005854, BG032749, BF977511, BE904376, AV751904, BG258904, AV716107, AV651801, BE897653, AW958723, AV757537, AU157013, A1608790, BE892495, AA768118, AA460582, BF572668, A1096596, BF687508, BG256721, AA775502, AA451982, AW014146, N47947, A1685295, BF515596, AW770423, BE350955, AA444107, BE883684, AW503758, AW263530, AA461508, A1150229, AA446029, AA939060, A1375970, A1025102, AA446302, AA416943,

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HCHAK72	951	106212 3	1 - 2109	15 - 2123	AA534591, AW104113, BF435137, AA922301, AI978874, AA528179, AI251446, AW193752, AI469095, AI686794, AA883068, AW970064, AW970877, AW970564, AW973116, AW970958, AW975425, AI865738, AW975409, AW979140, AW975987, AW971963, AA410788, AW975012, AU147162, AW976003, AW971068, AW500684, AI755214, AA847499, AW976008, AI754567, AI733856, BG250286, AI754105, AW969933, AW576251, AW979200, AA832145, AI683116, AW970875, AW970030, BG180976, AA228778, AI923052, AW471332, AA225406, AV738383, AW969751, AW328331, BE178231, AW974932, AI056177, AV695478, AI249688, BF832074, BF828714, AI609972, AW615504, AW979284, AW023111, AL135377, AW468009, AI457597, BE178064, AI017251, AI669421, BF724372, AA176978, AI697425, AA704393, AV764259, BE042511, AA630854, BE970985, AV763540, BE062478, AI693979, AW958962, AA579152, AW272294, BF917486, AA524616, AA644090, BE138594, AL079734, AL118925, AW131356, AW979096, BF724838, AI537800, AU146620, AA610433, AA503019, AV762633, AA535216, AI687343, BE742024, AI038304, AI049955, BF870792, AW971097, BF854308, AA584484, AW975634, BF821897, AI635028, AU147839, AW576485, AA536040, AA456924, AV732038, AV763550, AI049630, AA568314, AA176604, AA169245, AW973992, AV761647, BF681619, AW265688, AA583386, AI887235, AI792464, AI569100, AW969753, BE062476, AW979159, AV759518, AI446452, BF247318, BF826830, AI345695, AW327624, AV755593, BG054730, AW192599, AV760508, AF201380, AC015555, AP001746, AP001623, AL442167, AL163285, AP001610, AP001609, AL031311, AC009364, AC005399, AC020904, AC011497, AC005953, AC004883, AL133545, U52111, AC003071, AP001718, AL109804, AC018643, AF243527, AF124523, Z84466, AL353802, AC003684, Z86090, AL049758, AC006480, AC004659, AC018641, AC006088, AL050335, AL035587, AC005821, AF146367, AC008812, AF134726, AC005225, Z93015, AL133453, AC068799, AC020916, AC005409, AC009155, AL080317, AL033529, AL132765, AC008264, AC011489, AL035450, AC002504, Z82206, AC024247, AJ009611, AL024498, AC005522, AL117333, AI295844, AL049694, AC018738, AC005519, AC005231, AL121952, AL035659, AC005668, AC005048, AC007191, AC003070, AC010326, AP001748, AC007731, AL136303, AP002898, AC005500, AC006942, AC002492, AC011475, AC002310, AC005000, AC027319, AF111169, AD001502, AL117694, AL162272, AL138914, AC006994, AF030453, AP000144, AL117381, AL109967, AC004383, AP001435, AL031668, L78810,

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HPAME12	952	106213 9	1 - 4017	15 - 4031	AL520948, AL534150, BE379785, BE889460, AW951413, AI636742, BF109648, AW389540, AW157786, BF093583, AL534149, AA894354, AI928930, BE379858, AI809775, AW389539, AI340277, N98563, AL121544, AA643931, AI139344, N47725, AI475939, AA234514, AI191842, AI858268, AW163828, AI087225, AI054103, AI270307, AI929183, BF245490, H97227, BF690921, BF726007, BF086123, BF07543, BF089189, BF885026, BF885029, H26066, AI127553, BG167657, AA634930, BF885025, N32132, BF092903, F08681, BF885020, BF092933, AA635726, AL045202, BF885030, BE244005, BF377457, BF885023, BF086142, BF377423, BF092909, AI219134, AA298466, AA296906, AA953281, AI834343, AA657786, BF885024, AA658139, BF092910, BF092831, BF885015, AI795861, BF092892, BF092913, BF092893, BF377465, BF885027, H97226, BF885022, H03564, H03553, BF092854, C02607, BF092866, AA329567, BF092908, BF092850, H03474, BF885014, AA875932, BF092853, AI810192, N56801, BF092833, BF092858, W24246, BF092843, AI819883, BF092875, BF885018, Z40106, AW276669, BF756688, BF092904, BF092839, N47724, BF092845, AA376865, W87286, AA359837, BF377447, BE701352, BF092856, BF885005, and U34605.
HPCQK37	953	106226 0	1 - 1866	15 - 1880	AU120097, BE740116, AU121181, AI185118, BF981615, BG110591, BE546255, AL525287, BF312815, BG117879, BG032223, BE296715, BF313657, BE314543, BF980741, AA926785,

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				15 - 1537	AL514620, AL336205, AL523210, ALS37131, AL525645, AL521425, BF311286, BG258324, BG031889, BE891149, BF530602, BF182863, BF037516, BE560984, BE314805, BG027266,
			1 - 1523		
	954	106230			
HCE4F10					

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HBCBE63	955	106232 8	1 - 1688	15 - 1702	BF125787, BE729903, AW578276, BF868558, BE407151, AW044387, AI348180, AA878114, AW663931, AW578277, AW510900, BF880313, AW340635, AI436687, AI143954, AI343602, AI357253, BE386970, AI343568, AI951064, AI916581, AA513427, AA639505, AW205284, AA863186, AA992690, AI272767, AA758554, AA886199, BE504318, AI308813, BE872847, AA313762, AI659827, BG055204, AI784443, BF572882, BF742211, AA324486, AA506764, BG015015, AA135374, BE827464, AF007170, AL162430, AK000220, and AB007921.
HSSJO19	956	106234 6	1 - 1463	15 - 1477	BF664489, BG025594, BG103829, BG025801, BF036169, AI582833, BE669616, AW297031, BF434005, AI348145, AW003926, AI609194, AA826364, AI342910, AA483510, AA693913, R15864, R15863, AI675022, R34440, BF941111, AW504856, AA903163, AW237128, AA935221, AA557314, AW139232, R48974, BE300179, AA700361, AA094807, AA502939, AI886280, AA187873, AW403759, AA187874, AW846045, W74137, AW732231, AW731970, AA383361, AI126180, AI697181, AW250863, AW250109, BE905310, BE739570, F22239, AI076622, AA938975, AI874254, AI401662, AU158593, BE549170, AI797537, AI126903, AI904336, AI904341, AA575960, AA947516, AA604706, AA313272, AW875275, AI905921, AW247859, AV731835, AA570611, AL110193, AC007842, AC003693, AC004616, AJ006345,

HE8NQ23	957	106236 9	1 - 1776	15 - 1790	AL139150, AL133548, AL035106, AL356118, AL031655, AC020908, AC007676, AC068799, AC004966, T66490, and T66489.
HTELJ95	958	106243 1	1 - 1647	15 - 1661	AL962439, AA424098, AA460529, AI968199, AI367723, AI969765, AI699236, AI206192, AL530798, AI697103, AF062006, AF061444, AF110818, and AX016185. AU118298, BE739527, BE869231, BE739783, BG258670, AL047680, AU120304, BF207656, AW957634, BF692429, AU127515, BF666306, BF680361, BF692388, BF573293, BF208154, BF698175, BF666489, BF670276, BF698426, BF574553, BE379831, BF244412, BF211731, BF029813, BF244460, BF667117, AV711581, BF668580, BF184480, BF979219, BF694128, BF978578, BF979035, BF242514, BE379947, AW674926, BF668924, BF211442, AA085749, BE564271, AI161329, BF667604, AI458425, BF207943, BF027717, AV761666, BF028919, BE564668, BF668645, BF211078, BF700097, AV714512, BF208109, BF214772, BE566424, BF589406, AI220487, BF696815, BF245420, BE568677, BF061018, BE566650, BE866712, BF977541, BE566046, BF668139, BE569092, BF132230, BF79920, BG034292, AA312639, BF215159, BF215749, BF184533, BF700586, BF700982, BF697918, AU144893, AA935565, BE739263, BE960900, BF029561, BE379721, BF690901, BF214611, BF103768, AV704751, BF542116, BE739009, BF697833, BF590340, BE565639, AA160565, BE568609, BE970128, BF670029, BF664604, BE910213, BF029401, BF694228, BF029167, BF030210, AU150083, AA159916, AA505806, BF029651, BF244279, BF207497, BF666214, BF573752, BE972722, AW403249, BF027718, BF132908, BF576115, BF208561, BF669678, BE564803, BE568871, BF698949, AI671765, BE564945, BF240423, BF031415, AU146402, BE568687, BE564459, BF244906, AA954921, BF104963, AA128376, BF214943, BF184357, AI073761, AA947866, BF571840, BF677692, W07537, AA165026, AA805959, BF217335, AV661558, BF247837, BF217901, AI123292, BF675630, BF977328, AA825818, BE566776, AW674590, AA932330, BF130294, BE961174, AA810172, AA160253, H94797, AV739771, BF208724, BF574072, BF208041, BF030421, BF207805, BF131887, AA160252, BF570547, BE565834, BF571246, BE565094, C03597, BF029007, T19370, T78271, AA731306, BF695998, BE567717, AA907405, BE567475, N80741, C21337, AA147329, AA374477, BF241249, T78099, H48920, BF694245, BF246944, BE815523, BF028131, AA328225, BF246100, AA355205, AL047681, BF246005, AI719856, AI384085, N30715, BF214890, AV736109, AV742550, BF208176, AA774405, H48921, BF208535, BF217146, AV742551, BE855952, AW361432, N41329, BF209810, AA732085, BF208530, AA573751, BE326283, N56838, BF666070, BF671397, AI952391, AW797402, AW235332, AA328302, BF216221, BF209570, AA082421, N59836, AW391564, AV755858, AW973292, BF671547, AA186815, BF208983, BF242270, BF214287, BE565103, BF240920, AI732972, AI347472, AI791367, AA872247, BF208754, AA760959, AB006679, and AF027733.
HTPCP50	959	106243 5	1 - 2992	15 - 3006	AW959554, BE503321, BF439602, AA724866, AI241562, AI802994, BF679074, BF789905, W72803, AI024852, AI127443, W76329, AA429137, AA700716, AA487977, AW204065,



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HKGBU67	960	106249 6	1 - 765	15 - 779	BE537330, AI888137, AV701370, AU128929, BE613107, BE781577, AI672845, AW956358, BE962666, AI570562, AW440620, BF027216, AV701455, AA403116, BE612527, AI279867, AA418410, AW190186, BF794821, BE909695, AA401841, AU151145, AA905617, AW406511, AI798784, AA904054, AI401140, BF219013, AA887280, AI313194, AA081356, AI167620, AI018151, AI149369, AA593855, AI186137, AW070380, AA418507, BE958141, AA422027, AW136809, AI271520, AA833745, AA593915, AA461241, AI091023, AI672989, AA814928, N57462, W88723, AI285073, AI470105, AI476041, AI808738, AA639807, AV691385, AI023904, AV686945, AA025365, AA719755, W21365, T53949, BE547365, AA360441, AA338778, T55484, N29519, T55410, AA972490, AI968907, BE774710, AA356437, N93015, AA081355, AW137776, AA765233, AW795784, AA699446, W88724, BE502542, AI090475, AI913976, BF590992, AA872346, AA090282, AV712556, BE092555, AF016371, AF036331, and AL030995.
HFKIT82	961	106254 4	1 - 1848	15 - 1862	AW129420, AL526882, AI954625, BG252755, AW515637, AW002450, AI218958, AI075929, W72881, BE502304, BF344975, AI860065, AW510578, AI696337, BF341699, AA461147, AW772266, R14839, R14808, BF344755, AA666277, AI692833, W74406, BF108710, AI739359, HI1713, BE883297, H51918, AI826180, BE463846, AW029326, AA903644, AA913932, AI623196, BF949967, AW294155, R18323, C06135, AI969803, W23997, AI652903, AI954650, AI970097, BF511055, T80549, BF361444, R11697, AA535279, AA019283, AA883986, AA054103, AL138095, AI905980, H83974, BG115528, AI201698, AI219898, BF949569, AW025845, AA679116, AW881802, AI910215, AA437196, AW593514, AC005754, AC008688, AC025436, AFI52495, AFI52496, AFI52493, AC005752, AFI52490, AFI52491, AFI52497, AF282973, AF217757, AC074130, AB046841, AFI52502, AF217749, AR025266, AFI52494, AFI52501, AFI52498, AI117449, AFI52499, AFI52528, AFI52492, AFI52500, AK024641, AFI52489, AC020967, AC020974, AFI131761, AK023190, AR025265, AK021915, AFI52527, AC005618, AFI52507, AFI52318, AFI52510, AFI52323, AFI52509, AFI52508, AFI52513, AFI52322, AFI52326, AR025269, AB002325, AFI52515, AFI52328, and D88795.
HE2LW42	962	106257 4	1 - 1288	15 - 1302	AL042644, AV753036, AI174720, AV727351, AA777328, AI268349, AV688028, AI292216, AV729489, H59650, AV693628, R53767, AA744996, AI342797, BF056041, AW590055, AI337141, W07248, AV749927, AW590523, BG015185, AV723467, AI064754, AA318543, AI689792, BE046799, W88477, AI240743, H87083, AA699845, BF927790, AV748261, AV747610, R97197, R91627, H91969, AW148855, R99163, N92066, BF895065, H71305,

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HOGCE44	963	106258 6	1 - 2812	15 - 2826	<p>AI529207, AU131514, BF966725, AU118705, BG176867, BG260610, BF796807, AV725097, BG120210, BE890223, BE670805, BE891248, BG031774, BF691460, BE159045, BE159047, BF793410, BE620303, AI681703, AW857786, BE159033, BF968000, AU133714, BE694456, AW363349, AL133793, BE219535, BF976878, BF740139, AU145204, AI953648, BE892122, AA426391, BF881261, AU131939, BF083273, AW271550, AA599010, AW950106, AA932884, AI832044, BE620839, AI360263, AI332405, AL134494, BE218915, AW861560, AA489281, AU153590, AI480021, AI719025, AI554931, AA477783, AU154944, AA719830, BF038414, AI686963, BE813109, AW137641, BF081957, BF083263, AA829712, W00647, AW578909, AA836400, BF871460, AA305783, AV709911, BE895783, BE831167, AI041343, AW510304, BE702612, AI929319, AI718863, AA477395, AA477895, AW815726, AA045329, AA045387, W94959, R72051, AA486424, H08441, BF761351, BE936282, AA301683, AW118521, AI002196, AW613749, BF087893, T66094, R53499, F11788, AI868515, AA262364, AW802792, AI860943, AA372002, R53498, AW630161, AA341432, BF082195, AW842290, AW805858, H08727, BF748789, R73159, R09595, H82419, AW852196, BF920867, R73234, AA429305, AA994434, AI674319, N48502, AI526057, AW578911,</p>

					BE838646, BE819013, BE831001, AW901012, AW293085, BF768303, BE838677, BF359607, AA599125, BE830999, BE838586, BE819051, BE819053, T54000, BF944501, AI423048, AA358611, AV726372, BE830998, AA843689, N45506, BE830916, BF330106, BE830996, BF966656, AU153238, BF330110, AA707394, AI090208, BF371174, BE247047, AI814986, AV752167, BF343829, AI096352, BE830992, AI139084, R87597, D55167, H23531, AW630229, AA041424, AA878457, BE830994, T52556, AW815625, BE830960, N63319, BE005119, BE838663, BF761232, AA760997, BF327571, AI284972, AA614732, BF824790, AA164321, AA248397, R71899, AI312849, R09495, H23557, BE933359, AA356438, AA029778, AA642084, BE838644, AA363943, R21009, AA906966, BE933537, AA782084, BE830993, AI383363, M34668, I23846, X54130, X54890, X53364, I23847, I01702, M36033, L22437, Z32749, X54134, AL121905, AX033920, U57500, Z23054, Z23055, L13680, L13669, AB046072, L13674, L13675, L13677, L13668, L13672, L13681, L13684, and AX033934.
HOVJJ72	964	106262 6	1 - 2072	15 - 2086	BF685761, AI927486, BE781435, BE897367, BF437053, BE858728, BF348277, BG058683, AI674231, AI962534, BF726437, AI810612, AI923238, AW304824, AI338279, AW082888, BE257506, AA524737, AI339319, AI081760, AI138880, BF058141, AI565999, BF439557, AI680453, AI523996, AI342308, AW001338, AI952559, AA455886, AI421925, AI146722, AI274832, AI342562, BF128840, AV695313, AW205524, AI367531, AI263799, AI880114, AI798737, AI200656, AI650628, AI910869, AI674502, AI521083, AI925242, AI284195, BF129063, AI089196, AV693097, AI219515, AI880273, AW130599, BE677656, AA455883, AW079524, AI679856, AI865850, AA148540, BE503049, AA010344, AI679281, AI887554, AA632997, AI220656, AA194919, BF990462, AI634901, BF932272, AW188449, BF761164, AI808866, H26532, AI091957, R73631, AA134237, AI859881, AA194920, AA580244, AI194001, AA741176, AA832367, AI962066, BE938366, BE832299, AW190526, AI080370, AA777156, AA732832, AI185976, AA156632, H25720, AW190400, BF001400, AA400695, AI868623, R54677, AA148784, AI039261, W76189, BE938494, AW118247, AI581956, AV690144, AA743700, H40747, AI041507, AI278902, R66168, AW172445, AI199557, R54676, AW298684, H46427, AW242200, AW517309, BF115401, AI005082, AI243368, AI263274, AI563963, AI817986, AI365561, BE672981, AI494458, AI243614, AI365570, BF850280, AI538466, AA452870, AI580973, AA742664, AA864796, AI190958, BE677499, BF929130, N95346, AA705811, AI346405, AI589753, W72018, AI690402, AV691082, AV693294, AV688786, AV694416, AA913716, AA905648, R00343, N89911, AA993262, AV684738, AA918430, AI371509, AV686967, AI015415, H27241, N35381, AI089208, W72295, AA010345, AW196950, W72990, R50392, AA134236, AI825465, AW241576, R48919, AV692353, AI521081, AA150448, AV684528, AA411769, R48807, AA885408, AI932574, BF886497, H28547, AI884711, W76321, AI971315, W07358, BF447545, H26623, AI863830, BF794570, H46665, BG152791, BE616297, AI370906, R67050, BF360816, BF001377, BF476577, AI453016, AA877349, AI129195, H28546, R87406, AA736760, .

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HODBT14	965	106262 8	1 - 617	15 - 631	AV683488, AV652792, AV655669, AV698583, AV709265, AV688150, AV709232, AV962407, AV704853, AV729519, AV701525, AV697895, AV727101, AV695545, AV721972, AV704541, AV708440, AV705159, AV703106, AV705727, AV705611, AV707140, AV686405, AV702065, AV690209, AV707097, AW951773, AV725273, AV726103, AW952064, AV726716, AV706761, AW951711, AV731018, AV725697, AV758698, AV726503, AV707878, AV706975, AV704547, AV647006, AV702681, AV756755, AV706584, AV692600, AW950529, AV709987, AV686390, AV706443, AW963660, AV711518, AV703158, AV706893, AV704551, AV727015, AV713128, AW955616, AV703830, AV703715, AW964540, AV762343, AW954994, AV702296, AV707146, AV654711, AV649625, AW952328, AW958280, AV707733, AV726261, AV658334, AW963378, AV683053, AW950597, AI525316, AV693768, AW960237, AV705959, AV658770, AV728965, AW956619, AW952743, AV688407, AV703992, AV693604, AW957110, AV702298, AV695489, AV756799, AV728446, AV705216, AV708850, AV686420, T18597, AV758892, AV686100, AV695752, AV723685, AV726091, AV701545, AV649299, AV705520, AV709235, AV649305, AV709040, AV727828, AV689804, AV684811, AV687015, AV685675, AV693000, AW957853, AV727221, AV707236, AV691786, AW965813, AV755725, AV702515, AV703855, AV709141, AV685456, AV697039, AV647390, AV727052, AV694684, AV704973, AV726613, AV691080, AV728901, AW955713, AW958163, AW953802, AV727381, AW951707, AV727916, AW959366, AV701872, AV661369, AW953611, AW959994, AV706272, AV707217, AV705331, AW950047, AV763447, AV651519, AV706448, AV701751, AW960040, AV725375, AV728467, AV658299, AV683002, AW951184, AV694674, AV705909, AV691211, AV701754, AV724867, AV726362, AV693727, AV702172, AV651719, AV707359, AV704785, AV703460, AV710111, AV705319, AV684962, AV652528, AV704891, AV702277, AW958763, AV703821, AV705998, AV705777, AV653766, AW960658, AV684731, AV707631, AV726938, AA824604, AW959346, AV698400, AV725054, AW945144, AW963940, AV707572, AW962651, AW962388, AW960458, AV728853, AV694386, AW953645, AW953691, AW964673, AV707650, AV702947, AV688658, AW955708, AV697880, AV703978, AW958102, AV695359, AW960830, AV729348, AV705869, AV725948, AW951291, AW957533, AV684214, AV704392, AW949779, AL109758, L13858, AR061133, U94592, AX047064, Y09813, AX047063, A70869, AX047062, AF006072, AX009343, AX009341, AX009337, AX009335, AX009345, AX009342, AX009344, AX009340, AX009339, AX009336, AX009338,

						AX009334, AR050070, AR038762, A62298, A82595, A82593, Z30183, A62300, U45328, AF320628, AX040581, AX046743, and AR025466.
HBOEB83	966	106262 9	1 - 1380	15 - 1394		BF755445, W07601, BF843629, BF364932, BF840131, AA378282, R57499, AW384132, BF945921, BF943555, AA092071, Z19585, AF102887, X89963, AF152393, and L27263.
HODCT96	967	106263 1	1 - 529	15 - 543		BE064551, BF086062, BF893169, AK023721, D70831, AC010620, AC024563, AC012627, AC008990, AC004004, AB040906, AC011494, AC007204, AC008463, AC010329, M55422, AC011477, AC003973, and AC011493.
HTXJE60	968	106265 5	1 - 1550	15 - 1564		BF038124, BG171051, AW749929, AV732956, BE885891, BG119342, AW959370, BE384272, BF669153, BE410276, BE547057, BF514058, AV716716, BF666034, AW247514, BF243382, BF571380, N98593, AW361781, AA461153, BE409941, BF680949, R11877, H18036, AV682204, N36690, AA214548, H58648, AA584425, AW245099, A1192476, A1374760, W31019, A1086429, A1300181, R61663, R17754, A1376885, BF673383, A1199359, R17219, N24708, AA479642, AA291204, AA05250, AA629554, BF933763, AA362535, AA291660, AA745817, R67822, AA477330, AA213533, N79116, AW072748, A1262159, A1000698, A1936072, AA772228, AW992044, N54671, AW090390, BG230587, BF477852, AA973898, AW450684, A1632973, AK024756, and A1239531.
HUSIQ62	969	106267 9	1 - 1231	15 - 1245		AL527804, AL527803, AU133250, AL531642, AL531641, BG024567, BE409577, BE275235, BE900374, BE407097, BG110484, BG177580, BE733601, BF794754, BF796438, AU129699, BG257211, BF795405, BE277114, BF972712, A1207460, BE537036, BF976291, AW958534, A1802428, BG177394, BG113805, A1133236, BG180769, BG107198, BF981756, AV717659, AU129620, BE391607, AW951026, BE904310, BE255557, BG036677, BE252235, BE900713, BE408445, BE926573, BE782089, BG106443, BE389138, BE884653, BE279526, BE539248, BF685431, BF213044, BE885774, AW673780, AW204191, AW936182, BF035534, AW936216, AW936154, BF797205, BE540934, A1204084, BE386536, BE296097, A1798235, AW593018, A1017913, A1798966, BF000818, AW250100, AW799320, A1523803, AW582711, BF064032, AW571487, AW167852, AW327724, BF974778, AV754043, BE888728, BE394509, BF663406, AW605135, AA714394, BF912862, BE394384, AW936161, AW799305, BF683464, AU151712, BE394533, BG059618, BF184313, BE388631, BF211439, BE047170, AW605184, N31851, AU154621, AW291824, BF238052, BE882796, AW468394, A1831782, AW246077, AW440973, BE390283, A1954999, AW803951, A1380618, BE645929, A1434252, A1338618, A1369130, AA580516, A1373115, A1738431, A1336359, BE566233, AW327783, A1683060, BE885950, AW404086, A1242410, A152603, AW473412, A1432821, A1954175, BF028000, A1745038, A1905275, AA807713, AW605160, BF095616, A1126474, BF184229, A1270212, A1022067, AA806501, BE777563, W60824, AA629547, BE221418, AW674103, AA187362, A1355746, A1570979, N23950, A1033448, AA868159, AA766119, AA954820, BF913491, AA521127, AV714125, AW002354, A1355783, AA731362, AW608831, AW665939, AW406422, BE535671, AA969082, AW866948, W68241, BE328028,

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HPCTC48	970	106268 6	1 - 1099	15 - 1113	<p>AL518312, BE876206, BG249252, AW965671, BG117042, BF242380, AW965669, BF541503, BF214421, AI990836, BF030816, BF475708, AI360210, AW118735, AW241585, BF852809, AA159926, AI671624, AI918769, A668872, AI129365, BF002990, AI570207, AI921845, AA759100, AA608962, AI480175, AA534338, AA622034, AA128382, AW511429, BF244063, AW014932, BE350318, AW191019, AI632581, BF590946, BE551547, AI864862, AA962714, AI809654, AA195594, AW591626, AI917844, AW274989, BF574216, AA458988, AA564992, AW243373, AI244452, BE349611, F34378, AA459203, AV708611, AI239924, AA287277, BF672808, AA604658, AW675711, AA147341, BE865967, BG057896, D59283, AI962921, AW780340, AV708614, BE672924, H77893, AA191343, AA810152, BF675349, BE565472, AW024311, AW901422, BF852230, AV757324, AI368536, AW338999, AI619533, BF375145, AI701851, AA936959, BE618592, AA253008, AL518313, AI274509, AW904157, T35346, AW888698, T33750, AV682653, AI926285, BE706231, AW904146, Z42909, BE880505, AI366371, AI165037, AA626230, BF698473, N72642, AI761817, AW573584, N63390, AA629849, BE699232, AI832841, BF063350, AA852076, AV756635, AA194959, AV713926, BE565910, BF103813, AA069322, BE699283, BF669833, BF103883, BG256173, AA253132, AA287427, BG108565, N56321, BE958352, AW304692, AA659675, BF029358, AW337940, AA356559, BG249403, AW578864, AW904646, BF378777, AI860409, AW138982, BE172110, N58731, BF819096, BF058158, AW857007, AW371763, C00473, W27589, BE257642, BF514579, BG255384, BE765235, BE256501, BE889415, BE881408, BF081300, BG163413, AX018191, AL035305, AF314752, AX018169, Z99127, AF057356, AF275803, and U97327.</p>
HKBAK29	971	106271 8	1 - 2308	15 - 2322	<p>BE886739, BE379712, BG168115, BE738372, BE896807, BG025579, BF205840, AV713523, BE748565, BG256937, BF793599, AV715761, BG106972, BF695583, BE739467, BF239177,</p>

					AV705893, BE748150, BF103730, BF969127, BF701016, BF126330, BF244101, BE737904, BE884439, BG170672, BF698489, BE958039, BE738525, BE380151, BF791298, BE778335, BF574286, BG025350, BF692635, BF673154, BE878575, BF216818, BE565458, BE380095, BF665447, AV734153, BF677665, AW662229, BE564926, BF218156, BF028050, BF978882, BF218613, BF667003, BF130786, BF185082, BF698689, BF696054, BF244450, BE567375, BF697784, BF031300, BE865570, AW629584, BF028129, A1922913, BF184277, BF664732, BF218692, BE961009, BE568735, BF666910, BF695466, BF240106, AV731226, BF690657, BF977414, BF665136, BF696631, BE893984, BF436115, BF675422, A1339300, BF184615, BE881989, BF211735, BF699602, BF215527, BF692092, BF029085, A1983656, BF209826, BF240468, BF667839, AW167080, BF211689, BF791905, BF102749, BF248301, BF541104, BF244039, BF697329, BF218994, BF674179, BF691956, BF977851, BF185596, BF697826, BF185162, BE567330, BF245021, BF692317, BE567209, BF247040, BF540969, BE566194, BF692270, BE538457, BF245139, BE568536, AW020664, BE567726, BF241912, BF695669, BF217846, AW614845, BF446091, BF669512, BF028637, BE564037, BF240278, BF209701, BF698380, BF027884, BF700733, BF690815, A1458458, BE866044, BF027945, AW994882, BE566654, BF790759, BF102678, BF219415, A1802233, BF666381, BE567929, BF243653, AW007398, A1917870, BF240200, AA421623, AA931986, BF105024, A1612776, BE567167, A1061417, AA903250, BF240291, A1701592, A1459419, BE567930, BF245311, BF678201, BF243671, A1911672, A1458491, BF104786, BF572326, A1344531, AA826495, BF571127, AA528059, A1298139, A1080254, A1631363, BE737773, BF541077, BE739135, D55768, AW515524, BF185150, AA224330, BE931178, AA470080, BF888598, BE971070, N48726, BF207877, A1358628, A1278396, BF083962, AA864458, BF240912, BF239273, AV757587, D53475, A1081009, A1767667, AV743809, BF247295, AV761646, BF698069, BF216783, AV656347, A1536768, AV658919, D60350, BF033302, W52191, BE047925, A1536024, AA635842, BF218667, BF208790, BF676269, AW957445, H25618, BF211414, AA908466, A1435203, BE960800, A1279724, AW797393, BF693941, D60465, Z24859, A1300288, D81481, AA625143, AW385928, W52903, BF217163, N56293, T90076, BF240099, AA748884, AA353356, BE709325, BE709355, BF130723, AA037331, A1432717, BE738360, A1291624, AA319066, AA223798, AA247834, A1803923, D55769, BF357986, AA301101, A1872348, D54242, AF132968, AF161525, AK024753, AF275810, AF229832, Z58933, AF144082, C02225, and A1560591.
HPMCX26	972	106274 3	1 - 669	15 - 683	BE006225, BF038302, AA368470, A1820542, BF996462, BG010637, T64506, BF767592, BF830211, T93730, AC002073, AL117466, D45906, AB005131, U88618, AB008117, AB005132, D31874, D31875, D31876, D31877, AB005135, and D85527.
HFKHF51	973	106278 5	1 - 2428	15 - 2442	BE746374, A1743383, A1189480, AV728988, BE899408, BE562186, BE746781, BE561742, AV722367, BF347181, BE294788, BF530313, BE297333, BE397775, BF309493, BE268309, A1952007, BE743200, BE299126, AW952382, AW571554, AW130259, AW269905,

											<p>AW268367, BF310849, AI400646, BE857180, AI039861, AA639694, BF507388, AA994030, BF434700, AI056993, AW469101, AI280124, AW087805, AI040027, BF305457, AI095733, AA843902, AI813886, BF527954, AW043686, BE222971, AI018251, BE019740, BF727202, AW001144, AI184877, AA977540, AI221461, BF058113, AI744692, AA939338, BF058488, BE327064, AI631591, BF060991, AA884553, AI188291, BF111321, AW078707, AW300196, AI354719, AI362107, AA601020, AW239541, BF307205, AI961777, AA620650, AI971518, AA782108, AW468853, Z98493, AI123005, AI281234, AI371785, AI042264, Z98494, AI907175, BF945716, AA037644, AI983407, AI291368, AI189906, AI696796, AI805625, AI193049, AW068434, AA654142, AA028948, AI192226, AA424708, W86749, H18114, AA035346, BE902648, AW075664, AI085855, N50916, BF868739, BG152447, BF931509, AA137064, BF940371, AA584282, AI147886, AA082844, W65336, H03762, BF923686, AA621825, AI298050, R55061, AW068276, AA885454, AA954337, AA028947, BF929294, R48880, H50357, AA613635, BF871643, W96508, AV721662, AI991634, BF740062, AW051544, N26167, R74334, BF594397, W65306, N71800, AW067959, BE206342, H27911, AI750973, AI137135, N50788, AA984404, AA236213, AW015653, BF923702, AI744638, AV723825, AA419024, W35175, AA984360, R68793, AI741716, AI742212, R69300, N26168, R48488, AI991641, H02866, AI142695, AI468487, AA295172, H42461, T48913, R69284, R55030, AA668542, AA452705, H14200, AA022527, AI219145, AI475336, R48489, H18159, AI219092, R25771, R74427, H46438, AW014159, R69301, AW733005, BF357697, R69285, BF928802, AW444859, AA989514, H43664, BE702963, W87321, AA295171, T48912, AA904744, AI272234, W20398, AI085799, BF514530, AA083138, R48776, AA377483, R26607, AW581330, D59307, T12571, H42862, H44735, BF997408, AA358896, W96475, AV751736, BG014799, AI185266, H50395, AW068024, BE294110, BF932203, BF956105, N55145, AI915948, R73224, AA037643, AW834928, AA450064, AA236214, AA975214, BF941646, AW244038, BG007442, AA022459, R25786, AW578281, AW966531, AW978634, AV724520, AV699550, D58283, AV718692, AW975618, AV718489, AV699927, AW966053, AF177203, AB040935, AF218016, AC006312, AX047063, AX033851, A62298, A84916, A62300, AX027925, X67155, AR070327, AJ302649, AX047064, AX047062, AJ132110, AX020191, A67220, AX020190, AX021518, A23909, D26022, D34614, A78862, D89785, Y17188, AR018138, AR025207, AR092424, AX035434, X68127, D88547, X82626, AJ294956, AF058696, AB012117, AR088705, AF260572, AR008278, A85396, AR074141, AR066482, AX042372, A85477, AB028859, A86792, AR087649, X93549, AX015396, AX028130, I19525, AF135125, A82595, AJ287395, Y12724, AR074545, A44171, A30438, AR016808, AB037923, A94995, AR060385, AB002449, AR064240, I50126, AR008443, U79457, Y17187, I50132, I50128, I50133, AR066488, AR016514, AR060138, A45456, A26615, AR052274, AR008277, AR008281, AX035429, AX035428, AX035426, Y09669, AR074139, A43192, A43190, AR038669, AR066487, AR074136, D88507, X64588, AR066490, AR054175, I14842,</p>



HUCPE28	974	106279 5	1 - 1076	15 - 1090	AR016691, AR016690, U46128, D50010, I18367, AB033111, A63261, A70867, AR008408, AR091537, S69292, AR062872, Z32749, AR093385, I18371, X89963, D13509, A64136, A68321, AR060133, AR087528, A43601, I79511, S78798, U87247, AB023656, AF123263, AR032065, X98248, X93535, AR037157, AR008382, AA234577, and T19874.
					BE798851, A1762558, BE258902, BE251817, BE545676, AW967970, AW274241, BE855533, BE855590, AW242945, BF951715, AW027116, A1738977, A1097099, A1831606, A1935504, A1057522, AA243829, AW574617, A1361028, A1146329, AW275358, A1092427, A1089701, A1523606, A1097597, A1521322, AW511172, A1168266, A1807825, A1524209, A138290, A1660227, A1161303, AA954679, A1081418, BE502552, A1637508, AW137455, A1160335, A1523835, A1418882, A1076040, AA679406, AA855022, AW137563, A1018528, AW006211, A1027541, AW027121, AA994592, A1269258, AW135845, AA810915, BE857947, A1198243, AA455694, AA243750, A1698633, AA262194, A1537870, AW005460, A1651177, H87087, A1937020, AA873171, AA633518, AA835701, BF063722, AA765735, A1382433, A1039147, A1695656, AA813862, BE274246, AA846127, AA916726, AA749308, AA834567, AA766859, AA744763, AA884673, AW404490, R46413, AA764951, BG001430, AW138380, BE549583, AC008762, and AA808479.
HPWAH30	975	106284 0	1 - 817	15 - 831	AV755078, AU123448, AU143734, AU123664, BF797755, A1792344, A1566486, AW503073, BE064551, AV704018, BE396253, AU132789, A1733621, AA209235, BE897039, AV714960, AL042967, BF921029, BF699661, BF056061, BF749681, BG027032, AW976399, AW384427, AW859939, BE870310, BF773250, T47250, BF817669, A1554749, AA768909, A1744718, BE177809, AW272732, AW384913, N98899, AA397793, A1476267, AA743098, AA309966, BF749053, BF749575, AA976492, A1680077, AW502863, BE694276, BF240985, AU160228, T05813, AA480353, BF376299, BE177796, AA205471, BF748343, AA587596, BF921199, BE700971, AW105262, BF796887, A1718402, AA351793, A1280287, AA351526, A1049550, BF817370, A1241755, BE177799, BF751655, AA974841, BE694240, AW392975, A1042041, AW869565, T07738, AA352999, AW241205, T06856, AW887346, BE775238, BF247382, BE082118, L11672, AC016628, AC010329, AC021090, AC010620, AC012627, AC011477, AK023721, AC008554, AF070651, AC073539, AC011494, AC008626, X59244, AC022432, AC010636, AB040906, AC008739, AC024563, D70831, AC008463, X78932, AC008990, M27879, U35376, AB027251, AC011493, AC003973, AC008981, AC007204, AC011482, M55422, AC078899, Z96138, AL136969, AC004004, AL138715, AC006457, Z95704, AP000541, AC009006, L15309, AC006455, AC006539, AK022550, A1239321, AL163202, AF242519, AF054180, AF003540, AC000378, AC002519, U09847, AC025731, and AF038951.

**TABLE 4**

Code	Description	Tissue	Organ	Cell Line	Disease	Vector
AR022	a Heart	a Heart				
AR023	a Liver	a Liver				
AR024	a mammary gland	a mammary gland				
AR025	a Prostate	a Prostate				
AR026	a small intestine	a small intestine				
AR027	a Stomach	a Stomach				
AR028	Blood B cells	Blood B cells				
AR029	Blood B cells activated	Blood B cells activated				
AR030	Blood B cells resting	Blood B cells resting				
AR031	Blood T cells activated	Blood T cells activated				
AR032	Blood T cells resting	Blood T cells resting				
AR033	brain	brain				
AR034	breast	breast				
AR035	breast cancer	breast cancer				
AR036	Cell Line CAOV3	Cell Line CAOV3				
AR037	cell line PA-1	cell line PA-1				
AR038	cell line transformed	cell line transformed				
AR039	colon	colon				
AR040	colon (9808co65R)	colon (9808co65R)				
AR041	colon (9809co15)	colon (9809co15)				
AR042	colon cancer	colon cancer				
AR043	colon cancer (9808co64R)	colon cancer (9808co64R)				
AR044	colon cancer 9809co14	colon cancer 9809co14				
AR045	corn clone 5	corn clone 5				
AR046	corn clone 6	corn clone 6				
AR047	corn clone2	corn clone2				
AR048	corn clone3	corn clone3				
AR049	Corn Clone4	Corn Clone4				
AR050	Donor II B Cells 24hrs	Donor II B Cells 24hrs				
AR051	Donor II B Cells 72hrs	Donor II B Cells 72hrs				
AR052	Donor II B-Cells 24 hrs.	Donor II B-Cells 24 hrs.				
AR053	Donor II B-Cells 72hrs	Donor II B-Cells 72hrs				
AR054	Donor II Resting B Cells	Donor II Resting B Cells				
AR055	Heart	Heart				
AR056	Human Lung (clontech)	Human Lung (clontech)				
AR057	Human Mammary (clontech)	Human Mammary (clontech)				
AR058	Human Thymus (clontech)	Human Thymus (clontech)				
AR059	Jurkat (unstimulated)	Jurkat (unstimulated)				
AR060	Kidney	Kidney				
AR061	Liver	Liver				
AR062	Liver (Clontech)	Liver (Clontech)				

AR063	Lymphocytes chronic lymphocytic leukaemia	Lymphocytes chronic lymphocytic leukaemia				
AR064	Lymphocytes diffuse large B cell lymphoma	Lymphocytes diffuse large B cell lymphoma				
AR065	Lymphocytes follicular lymphoma	Lymphocytes follicular lymphoma				
AR066	normal breast	normal breast				
AR067	Normal Ovarian (4004901)	Normal Ovarian. (4004901)				
AR068	Normal Ovary 9508G045	Normal Ovary 9508G045				
AR069	Normal Ovary 9701G208	Normal Ovary 9701G208				
AR070	Normal Ovary 9806G005	Normal Ovary 9806G005				
AR071	Ovarian Cancer	Ovarian Cancer				
AR072	Ovarian Cancer (9702G001)	Ovarian Cancer (9702G001)				
AR073	Ovarian Cancer (9707G029)	Ovarian Cancer (9707G029)				
AR074	Ovarian Cancer (9804G011)	Ovarian Cancer (9804G011)				
AR075	Ovarian Cancer (9806G019)	Ovarian Cancer (9806G019)				
AR076	Ovarian Cancer (9807G017)	Ovarian Cancer (9807G017)				
AR077	Ovarian Cancer (9809G001)	Ovarian Cancer (9809G001)				
AR078	ovarian cancer 15799	ovarian cancer 15799				
AR079	Ovarian Cancer 17717AID	Ovarian Cancer 17717AID				
AR080	Ovarian Cancer 4004664B1	Ovarian Cancer 4004664B1				
AR081	Ovarian Cancer 4005315A1	Ovarian Cancer 4005315A1				
AR082	ovarian cancer 94127303	ovarian cancer 94127303				
AR083	Ovarian Cancer 96069304	Ovarian Cancer 96069304				
AR084	Ovarian Cancer 9707G029	Ovarian Cancer 9707G029				
AR085	Ovarian Cancer 9807G045	Ovarian Cancer 9807G045				
AR086	ovarian cancer 9809G001	ovarian cancer 9809G001				
AR087	Ovarian Cancer 9905C032RC	Ovarian Cancer 9905C032RC				
AR088	Ovarian cancer 9907 C00 3rd	Ovarian cancer 9907 C00 3rd				
AR089	Prostate	Prostate				
AR090	Prostate (clonotech)	Prostate (clonotech)				
AR091	prostate cancer	prostate cancer				
AR092	prostate cancer #15176	prostate cancer #15176				
AR093	prostate cancer #15509	prostate cancer #15509				

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AR094	prostate cancer #15673	prostate cancer #15673				
AR095	Small Intestine (Clontech)	Small Intestine (Clontech)				
AR096	Spleen	Spleen				
AR097	Thymus T cells activated	Thymus T cells activated				
AR098	Thymus T cells resting	Thymus T cells resting				
AR099	Tonsil	Tonsil				
AR100	Tonsil germinal center centroblast	Tonsil germinal center centroblast				
AR101	Tonsil germinal center B cell	Tonsil germinal center B cell				
AR102	Tonsil lymph node	Tonsil lymph node				
AR103	Tonsil memory B cell	Tonsil memory B cell				
AR104	Whole Brain	Whole Brain				
AR105	Xenograft ES-2	Xenograft ES-2				
AR106	Xenograft SW626	Xenograft SW626				
H0002	Human Adult Heart	Human Adult Heart	Heart			Uni-ZAP XR
H0003	Human Adult Liver	Human Adult Liver	Liver			Uni-ZAP XR
H0004	Human Adult Spleen	Human Adult Spleen	Spleen			Uni-ZAP XR
H0006	Human Frontal Lobe of Brain					Uni-ZAP XR
H0007	Human Cerebellum	Human Cerebellum	Brain			Uni-ZAP XR
H0008	Whole 6 Week Old Embryo					Uni-ZAP XR
H0009	Human Fetal Brain					Uni-ZAP XR
H0010	Human Fetal Hepatic	Human Fetal Liver	Liver			Uni-ZAP XR
H0011	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0012	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0013	Human 8 Week Whole Embryo	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0014	Human Gall Bladder	Human Gall Bladder	Gall Bladder			Uni-ZAP XR
H0015	Human Gall Bladder, fraction II	Human Gall Bladder	Gall Bladder			Uni-ZAP XR
H0016	Human Greater Omentum	Human Greater Omentum	peritoneum			Uni-ZAP XR
H0018	Human Greater Omentum, fII remake	Human Greater Omentum	peritoneum			Uni-ZAP XR
H0019	Human Fetal Heart	Human Fetal Heart	Heart			pBluescript
H0020	Human Hippocampus	Human Hippocampus	Brain			Uni-ZAP XR
H0021	Human Infant Adrenal Gland	Human Infant Adrenal Gland	Adrenal gland			Uni-ZAP XR
H0022	Jurkat Cells	Jurkat T-Cell Line				Lambda ZAP II
H0023	Human Fetal Lung					Uni-ZAP XR
H0024	Human Fetal Lung III	Human Fetal Lung	Lung			Uni-ZAP XR
H0025	Human Adult Lymph Node	Human Adult Lymph Node	Lymph Node			Lambda ZAP II
H0026	Namalwa Cells	Namalwa B-Cell Line, EBV immortalized				Lambda ZAP II
H0028	Human Old Ovary	Human Old Ovary	Ovary			pBluescript
H0029	Human Pancreas	Human Pancreas	Pancreas			Uni-ZAP XR

			s			
H0030	Human Placenta					Uni-ZAP XR
H0031	Human Placenta	Human Placenta	Placenta			Uni-ZAP XR
H0032	Human Prostate	Human Prostate	Prostate			Uni-ZAP XR
H0033	Human Pituitary	Human Pituitary				Uni-ZAP XR
H0034	Human Parathyroid Tumor	Human Parathyroid Tumor	Parathyroid		disease	Uni-ZAP XR
H0035	Human Salivary Gland	Human Salivary Gland	Salivary gland			Uni-ZAP XR
H0036	Human Adult Small Intestine	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0037	Human Adult Small Intestine	Human Adult Small Intestine	Small Int.			pBluescript
H0038	Human Testes	Human Testes	Testis			Uni-ZAP XR
H0039	Human Pancreas Tumor	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0040	Human Testes Tumor	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0041	Human Fetal Bone	Human Fetal Bone	Bone			Uni-ZAP XR
H0042	Human Adult Pulmonary	Human Adult Pulmonary	Lung			Uni-ZAP XR
H0044	Human Cornea	Human Cornea	eye			Uni-ZAP XR
H0045	Human Esophagus, Cancer	Human Esophagus, cancer	Esophagus		disease	Uni-ZAP XR
H0046	Human Endometrial Tumor	Human Endometrial Tumor	Uterus		disease	Uni-ZAP XR
H0047	Human Fetal Liver	Human Fetal Liver	Liver			Uni-ZAP XR
H0048	Human Pineal Gland	Human Pineal Gland				Uni-ZAP XR
H0049	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0050	Human Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0051	Human Hippocampus	Human Hippocampus	Brain			Uni-ZAP XR
H0052	Human Cerebellum	Human Cerebellum	Brain			Uni-ZAP XR
H0053	Human Adult Kidney	Human Adult Kidney	Kidney			Uni-ZAP XR
H0054	Human Corpus Colosum	Human Corpus Callosum	Brain			pBluescript
H0056	Human Umbilical Vein, Endo. remake	Human Umbilical Vein Endothelial Cells	Umbilical vein			Uni-ZAP XR
H0057	Human Fetal Spleen					Uni-ZAP XR
H0058	Human Thymus Tumor	Human Thymus Tumor	Thymus		disease	Lambda ZAP II
H0059	Human Uterine Cancer	Human Uterine Cancer	Uterus		disease	Lambda ZAP II
H0060	Human Macrophage	Human Macrophage	Blood	Cell Line		pBluescript
H0061	Human Macrophage	Human Macrophage	Blood	Cell Line		pBluescript
H0062	Human Thymus	Human Thymus	Thymus			Uni-ZAP XR
H0063	Human Thymus	Human Thymus	Thymus			Uni-ZAP XR
H0065	Human Esophagus, Normal	Human Esophagus, normal	Esophagus			Uni-ZAP XR
H0067	Human left hemisphere, adult	Human Left Hemisphere, Adult	Brain			Lambda ZAP II
H0068	Human Skin Tumor	Human Skin Tumor	Skin		disease	Uni-ZAP XR
H0069	Human Activated T-Cells	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0070	Human Pancreas	Human Pancreas	Pancreas			Uni-ZAP XR
H0071	Human Infant Adrenal	Human Infant	Adrenal			Uni-ZAP XR

	Gland	Adrenal Gland	gland			
H0073	Human Leiomyeloid Carcinoma	Human Leiomyeloid Carcinoma	Muscle		disease	Uni-ZAP XR
H0074	Human Platelets	Human Platelets	Blood	Cell Line		Uni-ZAP XR
H0075	Human Activated T-Cells (II)	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0077	Human Thymus Tumor	Human Thymus Tumor	Thymus		disease	Lambda ZAP II
H0078	Human Lung Cancer	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0079	Human Whole 7 Week Old Embryo (II)	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR
H0080	Human Whole 6 Week Old Embryo (II)	Human Whole Six Week Old Embryo	Embryo			Lambda ZAP II
H0081	Human Fetal Epithelium (Skin)	Human Fetal Skin	Skin			Uni-ZAP XR
H0082	Human Fetal Muscle	Human Fetal Muscle	Sk Muscle			Uni-ZAP XR
H0083	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Jurkat Cells				Uni-ZAP XR
H0084	Human Namalwa Membrane Bound Polysomes	Namalwa Cells				Uni-ZAP XR
H0085	Human Colon	Human Colon				Lambda ZAP II
H0086	Human epithelioid sarcoma	Epithelioid Sarcoma, muscle	Sk Muscle		disease	Uni-ZAP XR
H0087	Human Thymus	Human Thymus				pBluescript
H0090	Human T-Cell Lymphoma	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0092	Human Pancreas Tumor	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0093	Human Greater Omentum Tumor	Human Greater Omentum	peritoneum		disease	Uni-ZAP XR
H0095	Human Greater Omentum, RNA Remake	Human Greater Omentum	peritoneum			Uni-ZAP XR
H0096	Human Parotid Cancer	Human Parotid Cancer	Parotid		disease	Lambda ZAP II
H0097	Human Adult Heart, subtracted	Human Adult Heart	Heart			pBluescript
H0098	Human Adult Liver, subtracted	Human Adult Liver	Liver			Uni-ZAP XR
H0099	Human Lung Cancer, subtracted	Human Lung Cancer	Lung			pBluescript
H0100	Human Whole Six Week Old Embryo	Human Whole Six Week Old Embryo	Embryo			Uni-ZAP XR
H0101	Human 7 Weeks Old Embryo, subtracted	Human Whole 7 Week Old Embryo	Embryo			Lambda ZAP II
H0102	Human Whole 6 Week Old Embryo (II), subt	Human Whole Six Week Old Embryo	Embryo			pBluescript
H0103	Human Fetal Brain, subtracted	Human Fetal Brain	Brain			Uni-ZAP XR
H0105	Human Fetal Heart, subtracted	Human Fetal Heart	Heart			pBluescript
H0107	Human Infant Adrenal Gland, subtracted	Human Infant Adrenal Gland	Adrenal gland			pBluescript

H0108	Human Adult Lymph Node, subtracted	Human Adult Lymph Node	Lymph Node			Uni-ZAP XR
H0109	Human Macrophage, subtracted	Macrophage	Blood	Cell Line		pBluescript
H0110	Human Old Ovary, subtracted	Human Old Ovary	Ovary			pBluescript
H0111	Human Placenta, subtracted	Human Placenta	Placenta			pBluescript
H0112	Human Parathyroid Tumor, subtracted	Human Parathyroid Tumor	Parathyroid			pBluescript
H0113	Human skin Tumor, subtracted	Human Skin Tumor	Skin			Uni-ZAP XR
H0116	Human Thymus Tumor, subtracted	Human Thymus Tumor	Thymus			pBluescript
H0117	Human Uterine Cancer, subtracted	Human Uterine Cancer	Uterus			pBluescript
H0118	Human Adult Kidney	Human Adult Kidney	Kidney			Uni-ZAP XR
H0119	Human Pediatric Kidney	Human Pediatric Kidney	Kidney			Uni-ZAP XR
H0120	Human Adult Spleen, subtracted	Human Adult Spleen	Spleen			Uni-ZAP XR
H0121	Human Cornea, subtracted	Human Cornea	eye			Uni-ZAP XR
H0122	Human Adult Skeletal Muscle	Human Skeletal Muscle	Sk Muscle			Uni-ZAP XR
H0123	Human Fetal Dura Mater	Human Fetal Dura Mater	Brain			Uni-ZAP XR
H0124	Human Rhabdomyosarcoma	Human Rhabdomyosarcoma	Sk Muscle		disease	Uni-ZAP XR
H0125	Cem cells cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0128	Jurkat cells, thiouridine activated	Jurkat Cells				Uni-ZAP XR
H0129	Jurkat cells, thiouridine activated, fract II	Jurkat Cells				Uni-ZAP XR
H0130	LNCAP untreated	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0131	LNCAP + 0.3nM R1881	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0132	LNCAP + 30nM R1881	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0134	Raji Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0135	Human Synovial Sarcoma	Human Synovial Sarcoma	Synovium			Uni-ZAP XR
H0136	Supt Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0139	Activated T-Cells, 4 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0140	Activated T-Cells, 8 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0141	Activated T-Cells, 12 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0142	MCF7 Cell Line	MCF7 Cell line	Breast	Cell Line		Uni-ZAP XR
H0144	Nine Week Old Early Stage Human	9 Wk Old Early Stage Human	Embryo			Uni-ZAP XR

H0147	Human Adult Liver	Human Adult Liver	Liver			Uni-ZAP XR
H0149	7 Week Old Early Stage Human, subtracted	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR
H0150	Human Epididymus	Epididymis	Testis			Uni-ZAP XR
H0151	Early Stage Human Liver	Human Fetal Liver	Liver			Uni-ZAP XR
H0152	Early Stage Human Liver, fract (II)	Human Fetal Liver	Liver			Uni-ZAP XR
H0153	Human adult lymph node, subtracted	Human Adult Lymph Node	Lymph Node			Uni-ZAP XR
H0154	Human Fibrosarcoma	Human Skin Fibrosarcoma	Skin		disease	Uni-ZAP XR
H0155	Human Thymus, subtracted	Human Thymus Tumor	Thymus			pBluescript
H0156	Human Adrenal Gland Tumor	Human Adrenal Gland Tumor	Adrenal Gland		disease	Uni-ZAP XR
H0157	Activated T-Cells, 0 hrs, ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0158	Activated T-Cells, 4 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0159	Activated T-Cells, 8 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0160	Activated T-Cells, 12 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0161	Activated T-Cells, 24 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0163	Human Synovium	Human Synovium	Synovium			Uni-ZAP XR
H0164	Human Trachea Tumor	Human Trachea Tumor	Trachea		disease	Uni-ZAP XR
H0165	Human Prostate Cancer, Stage B2	Human Prostate Cancer, stage B2	Prostate		disease	Uni-ZAP XR
H0166	Human Prostate Cancer, Stage B2 fraction	Human Prostate Cancer, stage B2	Prostate		disease	Uni-ZAP XR
H0167	Activated T-Cells, 24 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0168	Human Prostate Cancer, Stage C	Human Prostate Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0169	Human Prostate Cancer, Stage C fraction	Human Prostate Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0170	12 Week Old Early Stage Human	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0171	12 Week Old Early Stage Human, II	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0172	Human Fetal Brain, random primed	Human Fetal Brain	Brain			Lambda ZAP II
H0173	Human Cardiomyopathy, RNA remake	Human Cardiomyopathy	Heart		disease	Uni-ZAP XR
H0175	H. Adult Spleen, ziplox					pSport1
H0176	CAMA1Ee Cell Line	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0177	CAMA1Ee Cell Line	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0178	Human Fetal Brain	Human Fetal Brain	Brain			Uni-ZAP XR
H0179	Human Neutrophil	Human Neutrophil	Blood	Cell Line		Uni-ZAP XR



H0180	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0181	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0182	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0183	Human Colon Cancer	Human Colon Cancer	Colon		disease	Uni-ZAP XR
H0184	Human Colon Cancer, metastasized to liver	Human Colon Cancer, metastasized to liver	Liver		disease	Lambda ZAP II
H0186	Activated T-Cell	T-Cells	Blood	Cell Line		Lambda ZAP II
H0187	Resting T-Cell	T-Cells	Blood	Cell Line		Lambda ZAP II
H0188	Human Normal Breast	Human Normal Breast	Breast			Uni-ZAP XR
H0189	Human Resting Macrophage	Human Macrophage/Monocytes	Blood	Cell Line		Uni-ZAP XR
H0190	Human Activated Macrophage (LPS)	Human Macrophage/Monocytes	Blood	Cell Line		Uni-ZAP XR
H0192	Cem Cells, cyclohexamide treated, subtracted	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0194	Human Cerebellum, subtracted	Human Cerebellum	Brain			pBluescript
H0196	Human Cardiomyopathy, subtracted	Human Cardiomyopathy	Heart			Uni-ZAP XR
H0197	Human Fetal Liver, subtracted	Human Fetal Liver	Liver			Uni-ZAP XR
H0199	Human Fetal Liver, subtracted, neg clone	Human Fetal Liver	Liver			Uni-ZAP XR
H0200	Human Greater Omentum, fract II remake,	Human Greater Omentum	peritoneum			Uni-ZAP XR
H0201	Human Hippocampus, subtracted	Human Hippocampus	Brain			pBluescript
H0202	Jurkat Cells, cyclohexamide treated, subtraction	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0204	Human Colon Cancer, subtracted	Human Colon Cancer	Colon			pBluescript
H0205	Human Colon Cancer, differential	Human Colon Cancer	Colon			pBluescript
H0207	LNCAP, differential expression	LNCAP Cell Line	Prostate	Cell Line		pBluescript
H0208	Early Stage Human Lung, subtracted	Human Fetal Lung	Lung			pBluescript
H0209	Human Cerebellum, differentially expressed	Human Cerebellum	Brain			Uni-ZAP XR
H0211	Human Prostate, differential expression	Human Prostate	Prostate			pBluescript
H0212	Human Prostate, subtracted	Human Prostate	Prostate			pBluescript
H0213	Human Pituitary, subtracted	Human Pituitary				Uni-ZAP XR

H0214	Raji cells, cyclohexamide treated, subtracted	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		pBluescript
H0215	Raji cells, cyclohexamide treated, differentially expressed	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		pBluescript
H0216	Supt cells, cyclohexamide treated, subtracted	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		pBluescript
H0217	Supt cells, cyclohexamide treated, differentially expressed	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		pBluescript
H0218	Activated T-Cells, 0hrs, subtracted	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0219	Activated T-Cells, 0hrs, differentially expressed	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0220	Activated T-Cells, 4 hrs, subtracted	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0222	Activated T-Cells, 8 hrs, subtracted	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0223	Activated T-Cells, 8 hrs, differentially expressed	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0224	Activated T-Cells, 12 hrs, subtracted	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0225	Activated T-Cells, 12hrs, differentially expressed	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0228	C7MCF7 cell line, estrogen treated	C7MCF7 Cell Line, estrogen treated	Breast	Cell Line		Uni-ZAP XR
H0229	Early Stage Human Brain, random primed	Early Stage Human Brain	Brain			Lambda ZAP II
H0230	Human Cardiomyopathy, diff exp	Human Cardiomyopathy	Heart		disease	Uni-ZAP XR
H0231	Human Colon, subtraction	Human Colon				pBluescript
H0232	Human Colon, differential expression	Human Colon				pBluescript
H0234	human colon cancer, metastatic to liver, differentially expressed	Human Colon Cancer, metastaticized to liver	Liver			pBluescript
H0235	Human colon cancer, metaticized to liver, subtraction	Human Colon Cancer, metastaticized to liver	Liver			pBluescript
H0238	Human Myometrium Leiomyoma	Human Myometrium Leiomyoma	Uterus		disease	Uni-ZAP XR
H0239	Human Kidney Tumor	Human Kidney Tumor	Kidney		disease	Uni-ZAP XR
H0240	C7MCF7 cell line, estrogen treated, Differential	C7MCF7 Cell Line, estrogen treated	Breast	Cell Line		Uni-ZAP XR
H0241	C7MCF7 cell line, estrogen treated, subtraction	C7MCF7 Cell Line, estrogen treated	Breast	Cell Line		Uni-ZAP XR
H0242	Human Fetal Heart, Differential (Fetal-Specific)	Human Fetal Heart	Heart			pBluescript

H0244	Human 8 Week Whole Embryo, subtracted	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0246	Human Fetal Liver-Enzyme subtraction	Human Fetal Liver	Liver			Uni-ZAP XR
H0247	Human Membrane Bound Polysomes-Enzyme Subtraction	Human Membrane Bound Polysomes	Blood	Cell Line		Uni-ZAP XR
H0249	HE7, subtracted by hybridization with E7 cDNA	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR
H0250	Human Activated Monocytes	Human Monocytes				Uni-ZAP XR
H0251	Human Chondrosarcoma	Human Chondrosarcoma	Cartilage		disease	Uni-ZAP XR
H0252	Human Osteosarcoma	Human Osteosarcoma	Bone		disease	Uni-ZAP XR
H0253	Human adult testis, large inserts	Human Adult Testis	Testis			Uni-ZAP XR
H0254	Breast Lymph node cDNA library	Breast Lymph Node	Lymph Node			Uni-ZAP XR
H0255	breast lymph node CDNA library	Breast Lymph Node	Lymph Node			Lambda ZAP II
H0256	HL-60, unstimulated	Human HL-60 Cells, unstimulated	Blood	Cell Line		Uni-ZAP XR
H0257	HL-60, PMA 4H	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0261	H. cerebellum, Enzyme subtracted	Human Cerebellum	Brain			Uni-ZAP XR
H0263	human colon cancer	Human Colon Cancer	Colon		disease	Lambda ZAP II
H0264	human tonsils	Human Tonsil	Tonsil			Uni-ZAP XR
H0265	Activated T-Cell (12hs)/Thiouridine labelledEco	T-Cells	Blood	Cell Line		Uni-ZAP XR
H0266	Human Microvascular Endothelial Cells, fract. A	HMEC	Vein	Cell Line		Lambda ZAP II
H0267	Human Microvascular Endothelial Cells, fract. B	HMEC	Vein	Cell Line		Lambda ZAP II
H0268	Human Umbilical Vein Endothelial Cells, fract. A	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0269	Human Umbilical Vein Endothelial Cells, fract. B	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0270	HPAS (human pancreas, subtracted)	Human Pancreas	Pancreas			Uni-ZAP XR
H0271	Human Neutrophil, Activated	Human Neutrophil - Activated	Blood	Cell Line		Uni-ZAP XR
H0272	HUMAN TONSILS, FRACTION 2	Human Tonsil	Tonsil			Uni-ZAP XR
H0274	Human Adult Spleen, fractionII	Human Adult Spleen	Spleen			Uni-ZAP XR
H0275	Human Infant Adrenal Gland, Subtracted	Human Infant Adrenal Gland	Adrenal gland			pBluescript
H0279	K562 cells	K562 Cell line	cell line	Cell Line		ZAP Express
H0280	K562 + PMA (36 hrs)	K562 Cell line	cell line	Cell Line		ZAP Express
H0281	Lymph node, abnorm.	Lymph Node,	Lymph	Cell Line		ZAP Express

	cell line (ATCC #7225)	abnormal cell line	Node			
H0282	HBGB's differential consolidation	Human Primary Breast Cancer	Breast			Uni-ZAP XR
H0284	Human OB MG63 control fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0286	Human OB MG63 treated (10 nM E2) fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0288	Human OB HOS control fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0290	Human OB HOS treated (1 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0292	Human OB HOS treated (10 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0293	WI 38 cells					Uni-ZAP XR
H0294	Amniotic Cells - TNF induced	Amniotic Cells - TNF induced	Placenta	Cell Line		Uni-ZAP XR
H0295	Amniotic Cells - Primary Culture	Amniotic Cells - Primary Culture	Placenta	Cell Line		Uni-ZAP XR
H0298	HCBB's differential consolidation	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0299	HCBA's differential consolidation	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0300	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express
H0305	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express
H0306	CD34 depleted Buffy Coat (Cord Blood)	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood			ZAP Express
H0309	Human Chronic Synovitis	Synovium, Chronic Synovitis/ Osteoarthritis	Synovium		disease	Uni-ZAP XR
H0310	human caudate nucleus	Brain	Brain			Uni-ZAP XR
H0313	human pleural cancer	pleural cancer			disease	pBluescript
H0316	HUMAN STOMACH	Human Stomach	Stomach			Uni-ZAP XR
H0318	HUMAN B CELL LYMPHOMA	Human B Cell Lymphoma	Lymph Node		disease	Uni-ZAP XR
H0320	Human frontal cortex	Human Frontal Cortex	Brain			Uni-ZAP XR
H0321	HUMAN SCHWANOMA	Schwanoma	Nerve		disease	Uni-ZAP XR
H0327	human corpus colosum	Human Corpus Callosum	Brain			Uni-ZAP XR
H0328	human ovarian cancer	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0329	Dermatofibrosarcoma Protuberance	Dermatofibrosarcoma Protuberans	Skin		disease	Uni-ZAP XR
H0330	HCBB's Subtractive (- mito genes)	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0331	Hepatocellular Tumor	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0333	Hemangiopericytoma	Hemangiopericytoma	Blood vessel		disease	Lambda ZAP II
H0334	Kidney cancer	Kidney Cancer	Kidney		disease	Uni-ZAP XR

H0339	Duodenum	Duodenum				Uni-ZAP XR
H0340	Corpus Callosum	Corpus Collosum-93052				Uni-ZAP XR
H0341	Bone Marrow Cell Line (RS4;11)	Bone Marrow Cell Line RS4;11	Bone Marrow	Cell Line		Uni-ZAP XR
H0343	stomach cancer (human)	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0344	Adipose tissue (human)	Adipose - 6825A (human)				Uni-ZAP XR
H0345	SKIN	Skin - 4000868H	Skin			Uni-ZAP XR
H0346	Brain-medulloblastoma	Brain (Medulloblastoma)-9405C006R	Brain		disease	Uni-ZAP XR
H0349	human adult liver cDNA library	Human Adult Liver	Liver			pCMVSPORT 1
H0350	Human Fetal Liver, mixed 10 & 14 week	Human Fetal Liver, mixed 10&14 Week	Liver			Uni-ZAP XR
H0351	Glioblastoma	Glioblastoma	Brain		disease	Uni-ZAP XR
H0352	wilm's tumor	Wilm's Tumor			disease	Uni-ZAP XR
H0354	Human Leukocytes	Human Leukocytes	Blood	Cell Line		pCMVSPORT 1
H0355	Human Liver	Human Liver, normal Adult				pCMVSPORT 1
H0356	Human Kidney	Human Kidney	Kidney			pCMVSPORT 1
H0357	H. Normalized Fetal Liver, II	Human Fetal Liver	Liver			Uni-ZAP XR
H0359	KMH2 cell line	KMH2				ZAP Express
H0360	Hemangiopericytoma	Hemangiopericytoma			disease	
H0361	Human rejected kidney	Human Rejected Kidney			disease	pBluescript
H0362	HeLa cell line	HELA CELL LINE				pSPORT1
H0363	Human Brain Medulla, subtracted	Human Brain Medulla				pBluescript
H0364	Human Osteoclastoma, excised	Human Osteoclastoma			disease	pBluescript
H0365	Osteoclastoma-normalized B	Human Osteoclastoma			disease	Uni-ZAP XR
H0366	L428 cell line	L428				ZAP Express
H0369	H. Atrophic Endometrium	Atrophic Endometrium and myometrium				Uni-ZAP XR
H0370	H. Lymph node breast Cancer	Lymph node with Met. Breast Cancer			disease	Uni-ZAP XR
H0372	Human Testes	Human Testes	Testis			pCMVSPORT 1
H0373	Human Heart	Human Adult Heart	Heart			pCMVSPORT 1
H0374	Human Brain	Human Brain				pCMVSPORT 1
H0375	Human Lung	Human Lung				pCMVSPORT 1
H0376	Human Spleen	Human Adult Spleen	Spleen			pCMVSPORT 1
H0379	Human Tongue, frac 1	Human Tongue				pSPORT1
H0380	Human Tongue, frac 2	Human Tongue				pSPORT1
H0381	Bone Cancer	Bone Cancer			disease	Uni-ZAP XR
H0383	Human Prostate BPH, re-excision	Human Prostate BPH				Uni-ZAP XR
H0384	Brain, Kozak	Human Brain				pCMVSPORT 1
H0385	H. Leukocytes, Kozak	Human Leukocytes	Blood	Cell Line		pCMVSPORT 1
H0386	Leukocyte and Lung; 4 screens	Human Leukocytes	Blood	Cell Line		pCMVSPORT 1
H0388	Human Rejected	Human Rejected			disease	pBluescript

	Kidney, 704 re-excision	Kidney				
H0390	Human Amygdala Depression, re-excision	Human Amygdala Depression			disease	pBluescript
H0391	H. Meningioma, M6	Human Meningioma	brain			pSport1
H0392	H. Meningioma, M1	Human Meningioma	brain			pSport1
H0393	Fetal Liver, subtraction II	Human Fetal Liver	Liver			pBluescript
H0394	A-14 cell line	Redd-Sternberg cell				ZAP Express
H0395	A1-CELL LINE	Redd-Sternberg cell				ZAP Express
H0396	L1 Cell line	Redd-Sternberg cell				ZAP Express
H0398	Human Newborn Bladder	Human Newborn Bladder				pBluescript
H0399	Human Kidney Cortex, re-rescue	Human Kidney Cortex				Lambda ZAP II
H0400	Human Striatum Depression, re-rescue	Human Brain, Striatum Depression	Brain			Lambda ZAP II
H0401	Human Pituitary, subtracted V	Human Pituitary				pBluescript
H0402	CD34 depleted Buffy Coat (Cord Blood), re-excision	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood			ZAP Express
H0403	H. Umbilical Vein Endothelial Cells, IL4 induced	HUVE Cells	Umbilical vein	Cell Line		Uni-ZAP XR
H0404	H. Umbilical Vein endothelial cells, uninduced	HUVE Cells	Umbilical vein	Cell Line		Uni-ZAP XR
H0405	Human Pituitary, subtracted VI	Human Pituitary				pBluescript
H0406	H Amygdala Depression, subtracted	Human Amygdala Depression				Uni-ZAP XR
H0408	Human kidney Cortex, subtracted	Human Kidney Cortex				pBluescript
H0409	H. Striatum Depression, subtracted	Human Brain, Striatum Depression	Brain			pBluescript
H0410	H. Male bladder, adult	H Male Bladder, Adult	Bladder			pSport1
H0411	H Female Bladder, Adult	Human Female Adult Bladder	Bladder			pSport1
H0412	Human umbilical vein endothelial cells, IL-4 induced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0413	Human Umbilical Vein Endothelial Cells, uninduced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0414	Ovarian Tumor I, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pSport1
H0415	H. Ovarian Tumor, II, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pCMVSPORT 2.0
H0416	Human Neutrophils, Activated, re-excision	Human Neutrophil - Activated	Blood	Cell Line		pBluescript
H0417	Human Pituitary, subtracted VIII	Human Pituitary				pBluescript
H0418	Human Pituitary, subtracted VII	Human Pituitary				pBluescript
H0419	Bone Cancer, re-excision	Bone Cancer				Uni-ZAP XR
H0421	Human Bone Marrow,	Bone Marrow				pBluescript

	re-excision					
H0422	T-Cell PHA 16 hrs	T-Cells	Blood	Cell Line		pSport1
H0423	T-Cell PHA 24 hrs	T-Cells	Blood	Cell Line		pSport1
H0424	Human Pituitary, subt IX	Human Pituitary				pBluescript
H0427	Human Adipose	Human Adipose, left hiplipoma				pSport1
H0428	Human Ovary	Human Ovary Tumor	Ovary			pSport1
H0429	K562 + PMA (36 hrs), re-excision	K562 Cell line	cell line	Cell Line		ZAP Express
H0431	H. Kidney Medulla, re-excision	Kidney medulla	Kidney			pBluescript
H0432	H. Kidney Pyramid	Kidney pyramids	Kidney			pBluescript
H0433	Human Umbilical Vein Endothelial cells, frac B, re-excision	HUVE Cells	Umbilical vein	Cell Line		pBluescript
H0434	Human Brain, striatum, re-excision	Human Brain, Striatum				pBluescript
H0435	Ovarian Tumor 10-3-95	Ovarian Tumor, OV350721	Ovary			pCMVSPORT 2.0
H0436	Resting T-Cell Library, II	T-Cells	Blood	Cell Line		pSport1
H0437	H Umbilical Vein Endothelial Cells, frac A, re-excision	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0438	H. Whole Brain #2, re-excision	Human Whole Brain #2				ZAP Express
H0439	Human Eosinophils	Eosinophils				pBluescript
H0440	FGF enriched mixed library	Mixed libraries				pCMVSPORT 1
H0441	H. Kidney Cortex, subtracted	Kidney cortex	Kidney			pBluescript
H0442	H. Striatum Depression, subt II	Human Brain, Striatum Depression	Brain			pBluescript
H0443	H. Adipose, subtracted	Human Adipose, left hiplipoma				pSport1
H0444	Spleen metastatic melanoma	Spleen, Metastatic malignant melanoma	Spleen		disease	pSport1
H0445	Spleen, Chronic lymphocytic leukemia	Human Spleen, CLL	Spleen		disease	pSport1
H0447	Salivary gland, re-excision	Human Salivary Gland	Salivary gland			Uni-ZAP XR
H0448	Salivary gland, subtracted	Human Salivary Gland	Salivary gland			Lambda ZAP II
H0449	CD34+ cell, I	CD34 positive cells				pSport1
H0450	CD34+cells, II	CD34 positive cells				pCMVSPORT 2.0
H0453	H. Kidney Pyramid, subtracted	Kidney pyramids	Kidney			pBluescript
H0455	H. Striatum Depression, subt	Human Brain, Striatum Depression	Brain			pBluescript
H0457	Human Eosinophils	Human Eosinophils				pSport1
H0458	CD34+ cell, I, frac II	CD34 positive cells				pSport1
H0459	CD34+cells, II, FRACTION 2	CD34 positive cells				pCMVSPORT 2.0
H0461	H. Kidney Medulla, subtracted	Kidney medulla	Kidney			pBluescript

H0462	H. Amygdala Depression, subtracted		Brain			pBluescript
H0477	Human Tonsil, Lib 3	Human Tonsil	Tonsil			pSport1
H0478	Salivary Gland, Lib 2	Human Salivary Gland	Salivary gland			pSport1
H0479	Salivary Gland, Lib 3	Human Salivary Gland	Salivary gland			pSport1
H0483	Breast Cancer cell line, MDA 36	Breast Cancer Cell line, MDA 36				pSport1
H0484	Breast Cancer Cell line, angiogenic	Breast Cancer Cell line, Angiogenic, 36T3				pSport1
H0485	Hodgkin's Lymphoma I	Hodgkin's Lymphoma I			disease	pCMVSPORT 2.0
H0486	Hodgkin's Lymphoma II	Hodgkin's Lymphoma II			disease	pCMVSPORT 2.0
H0487	Human Tonsils, lib I	Human Tonsils				pCMVSPORT 2.0
H0488	Human Tonsils, Lib 2	Human Tonsils				pCMVSPORT 2.0
H0489	Crohn's Disease	Ileum	Intestine		disease	pSport1
H0490	HL-60, untreated, subtracted	Human HL-60 Cells, unstimulated	Blood	Cell Line		Uni-ZAP XR
H0491	HL-60, PMA 4H, subtracted	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0492	HL-60, RA 4h, Subtracted	HL-60 Cells, RA stimulated for 4H	Blood	Cell Line		Uni-ZAP XR
H0494	Keratinocyte	Keratinocyte				pCMVSPORT 2.0
H0497	HEL cell line	HEL cell line		HEL 92.1.7		pSport1
H0504	CAPFINDER, Crohn's Disease, lib 2	Ileum	Intestine		disease	pCMVSPORT 2.0
H0505	Human Astrocyte	Human Astrocyte				pSport1
H0506	Ulcerative Colitis	Colon	Colon			pSport1
H0509	Liver, Hepatoma	Human Liver, Hepatoma, patient 8	Liver		disease	pCMVSPORT 3.0
H0510	Human Liver, normal	Human Liver, normal, Patient # 8	Liver			pCMVSPORT 3.0
H0512	Keratinocyte, lib 3	Keratinocyte				pCMVSPORT 2.0
H0517	Nasal polyps	Nasal polyps				pCMVSPORT 2.0
H0518	pBMC stimulated w/ poly I/C	pBMC stimulated with poly I/C				pCMVSPORT 3.0
H0519	NTERA2, control	NTERA2, Teratocarcinoma cell line				pCMVSPORT 3.0
H0520	NTERA2 + retinoic acid, 14 days	NTERA2, Teratocarcinoma cell line				pSport1
H0521	Primary Dendritic Cells, lib 1	Primary Dendritic cells				pCMVSPORT 3.0
H0522	Primary Dendritic cells, frac 2	Primary Dendritic cells				pCMVSPORT 3.0
H0523	Primary Dendritic cells, CapFinder2, frac 1	Primary Dendritic cells				pSport1
H0524	Primary Dendritic	Primary Dendritic				pSport1



	Cells, CapFinder, frac 2	cells				
H0525	PCR, pBMC I/C treated	pBMC stimulated with poly I/C				PCR II
H0529	Myeloid Progenitor Cell Line	TF-1 Cell Line; Myeloid progenitor cell line				pCMVSPORT 3.0
H0530	Human Dermal Endothelial Cells, untreated	Human Dermal Endothelial Cells; untreated				pSport1
H0533	Human Stromal endometrial fibroblasts, treated w/ estradiol	Human Stromal endometrial fibroblasts, treated w/				pSport1
H0534	Human Stromal endometrial fibroblasts, treated with progesterone	Human Stromal endometrial fibroblasts, treated w/				pSport1
H0535	Human ovary tumor cell OV350721	Ovarian Tumor, OV350721	Ovary		disease	pSport1
H0537	H. Primary Dendritic Cells, lib 3	Primary Dendritic cells				pCMVSPORT 2.0
H0538	Merkel Cells	Merkel cells	Lymph node			pSport1
H0539	Pancreas Islet Cell Tumor	Pancreas Islet Cell Tumour	Pancreas		disease	pSport1
H0540	Skin, burned	Skin, leg burned	Skin			pSport1
H0542	T Cell helper I	Helper T cell				pCMVSPORT 3.0
H0543	T cell helper II	Helper T cell				pCMVSPORT 3.0
H0544	Human endometrial stromal cells	Human endometrial stromal cells				pCMVSPORT 3.0
H0545	Human endometrial stromal cells-treated with progesterone	Human endometrial stromal cells-treated with proge				pCMVSPORT 3.0
H0546	Human endometrial stromal cells-treated with estradiol	Human endometrial stromal cells-treated with estra				pCMVSPORT 3.0
H0547	NTERA2 teratocarcinoma cell line+retinoic acid (14 days)	NTERA2, Teratocarcinoma cell line				pSport1
H0549	H. Epididymus, caput & corpus	Human Epididymus, caput and corpus				Uni-ZAP XR
H0550	H. Epididymus, cauda	Human Epididymus, cauda				Uni-ZAP XR
H0551	Human Thymus Stromal Cells	Human Thymus Stromal Cells				pCMVSPORT 3.0
H0552	Signal trap, Femur Bone Marrow, pooled	Femur Bone marrow, pooled from 8 male/female				Other
H0553	Human Placenta	Human Placenta				pCMVSPORT 3.0
H0555	Rejected Kidney, lib 4	Human Rejected Kidney	Kidney		disease	pCMVSPORT 3.0
H0556	Activated T-cell(12h)/Thiouridine-re-excision	T-Cells	Blood	Cell Line		Uni-ZAP XR

H0559	HL-60, PMA 4H, re-excision	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0560	KMH2	KMH2				pCMVSPORT 3.0
H0561	L428	L428				pCMVSPORT 3.0
H0562	Human Fetal Brain, normalized c5-11-26	Human Fetal Brain				pCMVSPORT 2.0
H0563	Human Fetal Brain, normalized 50021F	Human Fetal Brain				pCMVSPORT 2.0
H0564	Human Fetal Brain, normalized C5001F	Human Fetal Brain				pCMVSPORT 2.0
H0565	Human Fetal Brain, normalized 100024F	Human Fetal Brain				pCMVSPORT 2.0
H0566	Human Fetal Brain, normalized c50F	Human Fetal Brain				pCMVSPORT 2.0
H0567	Human Fetal Brain, normalized A5002F	Human Fetal Brain				pCMVSPORT 2.0
H0569	Human Fetal Brain, normalized CO	Human Fetal Brain				pCMVSPORT 2.0
H0570	Human Fetal Brain, normalized C500H	Human Fetal Brain				pCMVSPORT 2.0
H0571	Human Fetal Brain, normalized C500HE	Human Fetal Brain				pCMVSPORT 2.0
H0572	Human Fetal Brain, normalized AC5002	Human Fetal Brain				pCMVSPORT 2.0
H0574	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0575	Human Adult Pulmonary; re-excision	Human Adult Pulmonary	Lung			Uni-ZAP XR
H0576	Resting T-Cell; re-excision	T-Cells	Blood	Cell Line		Lambda ZAP II
H0578	Human Fetal Thymus	Fetal Thymus	Thymus			pSPORT1
H0579	Pericardium	Pericardium	Heart			pSPORT1
H0580	Dendritic cells, pooled	Pooled dendritic cells				pCMVSPORT 3.0
H0581	Human Bone Marrow, treated	Human Bone Marrow	Bone Marrow			pCMVSPORT 3.0
H0583	B Cell lymphoma	B Cell Lymphoma	B Cell		disease	pCMVSPORT 3.0
H0584	Activated T-cells, 24 hrs, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0585	Activated T-Cells, 12 hrs, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0586	Healing groin wound, 6.5 hours post incision	healing groin wound, 6.5 hours post incision - 2/	groin		disease	pCMVSPORT 3.0
H0587	Healing groin wound; 7.5 hours post incision	Groin-2/19/97	groin		disease	pCMVSPORT 3.0
H0589	CD34 positive cells (cord blood), re-ex	CD34 Positive Cells	Cord Blood			ZAP Express
H0590	Human adult small intestine, re-excision	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0591	Human T-cell lymphoma; re-excision	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0592	Healing groin wound - zero hr post-incision (control)	HGS wound healing project; abdomen			disease	pCMVSPORT 3.0
H0593	Olfactory	Olfactory epithelium				pCMVSPORT

	epithelium;nasalcavity	from roof of left nasal cavity				3.0
H0594	Human Lung Cancer;re-excision	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0595	Stomach cancer (human);re-excision	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0596	Human Colon Cancer;re-excision	Human Colon Cancer	Colon			Lambda ZAP II
H0597	Human Colon; re-excision	Human Colon				Lambda ZAP II
H0598	Human Stomach;re-excision	Human Stomach	Stomach			Uni-ZAP XR
H0599	Human Adult Heart;re-excision	Human Adult Heart	Heart			Uni-ZAP XR
H0600	Healing Abdomen wound;70&90 min post incision	Abdomen			disease	pCMVSPORT 3.0
H0601	Healing Abdomen Wound;15 days post incision	Abdomen			disease	pCMVSPORT 3.0
H0602	Healing Abdomen Wound;21&29 days post incision	Abdomen			disease	pCMVSPORT 3.0
H0604	Human Pituitary, re-excision	Human Pituitary				pBluescript
H0606	Human Primary Breast Cancer;re-excision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0607	H.Leukocytes, normalized cot 50A3	H.Leukocytes				pCMVSPORT 1
H0608	H. Leukocytes, control	H.Leukocytes				pCMVSPORT 1
H0609	H. Leukocytes, normalized cot > 500A	H.Leukocytes				pCMVSPORT 1
H0610	H. Leukocytes, normalized cot 5A	H.Leukocytes				pCMVSPORT 1
H0611	H. Leukocytes, normalized cot 500 B	H.Leukocytes				pCMVSPORT 1
H0612	H.Leukocytes, normalized cot 50 B	H.Leukocytes				pCMVSPORT 1
H0613	H.Leukocytes, normalized cot 5B	H.Leukocytes				pCMVSPORT 1
H0614	H. Leukocytes, normalized cot 500 A	H.Leukocytes				pCMVSPORT 1
H0615	Human Ovarian Cancer Reexcision	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0616	Human Testes, Reexcision	Human Testes	Testis			Uni-ZAP XR
H0617	Human Primary Breast Cancer Reexcision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0618	Human Adult Testes, Large Inserts, Reexcision	Human Adult Testis	Testis			Uni-ZAP XR
H0619	Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0620	Human Fetal Kidney; Reexcision	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0622	Human Pancreas Tumor; Reexcision	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0623	Human Umbilical Vein; Reexcision	Human Umbilical Vein Endothelial Cells	Umbilical vein			Uni-ZAP XR

H0624	12 Week Early Stage Human II; Reexcision	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0625	Ku 812F Basophils Line	Ku 812F Basophils				pSport1
H0626	Saos2 Cells; Untreated	Saos2 Cell Line; Untreated				pSport1
H0627	Saos2 Cells; Vitamin D3 Treated	Saos2 Cell Line; Vitamin D3 Treated				pSport1
H0628	Human Pre-Differentiated Adipocytes	Human Pre-Differentiated Adipocytes				Uni-ZAP XR
H0629	Human Leukocyte, control #2	Human Normalized leukocyte				pCMVSPORT 1
H0630	Human Leukocytes, normalized control #4	Human Normalized leukocyte				pCMVSPORT 1
H0631	Saos2, Dexamethosone Treated	Saos2 Cell Line; Dexamethosone Treated				pSport1
H0632	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver			Lambda ZAP II
H0633	Lung Carcinoma A549 TNFalpha activated	TNFalpha activated A549--Lung Carcinoma			disease	pSport1
H0634	Human Testes Tumor, re-excision	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0635	Human Activated T-Cells, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0637	Dendritic Cells From CD34 Cells	Dendritic cells from CD34 cells				pSport1
H0638	CD40 activated monocyte dendritic cells	CD40 activated monocyte dendritic cells				pSport1
H0639	Ficoll Human Stromal Cells, 5Fu treated	Ficoll Human Stromal Cells, 5Fu treated				Other
H0640	Ficoll Human Stromal Cells, Untreated	Ficoll Human Stromal Cells, Untreated				Other
H0641	LPS activated derived dendritic cells	LPS activated monocyte derived dendritic cells				pSport1
H0642	Hep G2 Cells, lambda library	Hep G2 Cells				Other
H0643	Hep G2 Cells, PCR library	Hep G2 Cells				Other
H0644	Human Placenta (re-excision)	Human Placenta	Placenta			Uni-ZAP XR
H0645	Fetal Heart, re-excision	Human Fetal Heart	Heart			Uni-ZAP XR
H0646	Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma,	Metastatic squamous cell lung carcinoma, poorly di				pSport1
H0647	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	Invasive poorly differentiated lung adenocarcinoma			disease	pSport1
H0648	Ovary, Cancer:	Papillary Cstic			disease	pSport1

	(4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot	neoplasm of low malignant potentia				
H0649	Lung, Normal: (4005313 B1)	Normal Lung				pSport1
H0650	B-Cells	B-Cells				pCMVSPORT 3.0
H0651	Ovary, Normal: (9805C040R)	Normal Ovary				pSport1
H0652	Lung, Normal: (4005313 B1)	Normal Lung				pSport1
H0653	Stromal Cells	Stromal Cells				pSport1
H0654	Lung, Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic lung adenoc	Metastatic Squamous cell lung Carcinoma poorly dif				Other
H0656	B-cells (unstimulated)	B-cells (unstimulated)				pSport1
H0657	B-cells (stimulated)	B-cells (stimulated)				pSport1
H0658	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	9809C332- Poorly differentiate	Ovary & Fallopia n Tubes		disease	pSport1
H0659	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	Grade II Papillary Carcinoma, Ovary	Ovary		disease	pSport1
H0660	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	Poorly differentiated carcinoma, ovary			disease	pSport1
H0661	Breast, Cancer: - (4004943 A5)	Breast cancer			disease	pSport1
H0662	Breast, Normal: (4005522B2)	Normal Breast - #4005522(B2)	Breast			pSport1
H0663	Breast, Cancer: (4005522 A2)	Breast Cancer - #4005522(A2)	Breast		disease	pSport1
H0664	Breast, Cancer: (9806C012R)	Breast Cancer	Breast		disease	pSport1
H0665	Stromal cells 3.88	Stromal cells 3.88				pSport1
H0666	Ovary, Cancer: (4004332 A2)	Ovarian Cancer, Sample #4004332A2			disease	pSport1
H0667	Stromal cells(HBM3.18)	Stromal cell(HBM 3.18)				pSport1
H0668	stromal cell clone 2.5	stromal cell clone 2.5				pSport1
H0669	Breast, Cancer: (4005385 A2)	Breast Cancer (4005385A2)	Breast			pSport1
H0670	Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	Ovarian Cancer - 4004650A3				pSport1
H0671	Breast, Cancer: (9802C02OE)	Breast Cancer- Sample # 9802C02OE				pSport1
H0672	Ovary, Cancer: (4004576 A8)	Ovarian Cancer(4004576A8)	Ovary			pSport1
H0673	Human Prostate	Human Prostate	Prostate			Uni-ZAP XR

	Cancer, Stage B2; re-excision	Cancer, stage B2				
H0674	Human Prostate Cancer, Stage C; re-excision	Human Prostate Cancer, stage C	Prostate			Uni-ZAP XR
H0675	Colon, Cancer: (9808C064R)	Colon Cancer 9808C064R				pCMVSPORT 3.0
H0676	Colon, Cancer: (9808C064R)-total RNA	Colon Cancer 9808C064R				pCMVSPORT 3.0
H0677	TNFR degenerate oligo	B-Cells				PCR II
H0678	screened clones from placental library	Placenta	Placenta			Other
H0682	Serous Papillary Adenocarcinoma	serous papillary adenocarcinoma (9606G304SPA3B)				pCMVSPORT 3.0
H0683	Ovarian Serous Papillary Adenocarcinoma	Serous papillary adenocarcinoma, stage 3C (9804G01)				pCMVSPORT 3.0
H0684	Serous Papillary Adenocarcinoma	Ovarian Cancer- 9810G606	Ovaries			pCMVSPORT 3.0
H0685	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-3	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-				pCMVSPORT 3.0
H0686	Adenocarcinoma of Ovary, Human Cell Line	Adenocarcinoma of Ovary, Human Cell Line, # SW-626				pCMVSPORT 3.0
H0687	Human normal ovary(#9610G215)	Human normal ovary(#9610G215)	Ovary			pCMVSPORT 3.0
H0688	Human Ovarian Cancer(#9807G017)	Human Ovarian cancer(#9807G017), mRNA from Maura Ru				pCMVSPORT 3.0
H0689	Ovarian Cancer	Ovarian Cancer, #9806G019				pCMVSPORT 3.0
H0690	Ovarian Cancer, # 9702G001	Ovarian Cancer, #9702G001				pCMVSPORT 3.0
H0691	Normal Ovary, #9710G208	normal ovary, #9710G208				pCMVSPORT 3.0
H0692	BLyS Receptor from Expression Cloning	B Cell Lymphoma	B Cell			pCMVSPORT 3.0
H0693	Normal Prostate #ODQ3958EN	Normal Prostate Tissue # ODQ3958EN				pCMVSPORT 3.0
H0694	Prostate gland adenocarcinoma	Prostate gland, adenocarcinoma, mod/diff, gleason	prostate gland			pCMVSPORT 3.0
H0695	mononucleocytes from patient	mononucleocytes from patient at Shady Grove Hospit				pCMVSPORT 3.0
N0006	Human Fetal Brain	Human Fetal Brain				
N0007	Human Hippocampus	Human Hippocampus				
N0008	Human Hippocampus, subtracted	Human Hippocampus				
N0009	Human Hippocampus, prescreened	Human Hippocampus				
N0011	Human Brain	Human Brain				
S0001	Brain frontal cortex	Brain frontal cortex	Brain			Lambda ZAP

						II
S0002	Monocyte activated	Monocyte-activated	blood	Cell Line		Uni-ZAP XR
S0003	Human Osteoclastoma	Osteoclastoma	bone		disease	Uni-ZAP XR
S0004	Prostate	Prostate BPH	Prostate			Lambda ZAP II
S0005	Heart	Heart-left ventricle	Heart			pCDNA
S0006	Neuroblastoma	Human Neural Blastoma			disease	pCDNA
S0007	Early Stage Human Brain	Human Fetal Brain				Uni-ZAP XR
S0008	Osteoclastoma	Osteoclastoma	bone		disease	Uni-ZAP XR
S0010	Human Amygdala	Amygdala				Uni-ZAP XR
S0011	STROMAL - OSTEOCLASTOMA	Osteoclastoma	bone		disease	Uni-ZAP XR
S0013	Prostate	Prostate	prostate			Uni-ZAP XR
S0014	Kidney Cortex	Kidney cortex	Kidney			Uni-ZAP XR
S0015	Kidney medulla	Kidney medulla	Kidney			Uni-ZAP XR
S0016	Kidney Pyramids	Kidney pyramids	Kidney			Uni-ZAP XR
S0021	Whole brain	Whole brain	Brain			ZAP Express
S0022	Human Osteoclastoma Stromal Cells - unamplified	Osteoclastoma Stromal Cells				Uni-ZAP XR
S0023	Human Kidney Cortex - unamplified	Human Kidney Cortex				
S0024	Human Kidney Medulla - unamplified	Human Kidney Medulla				
S0025	Human Kidney Pyramids - unamplified	Human Kidney Pyramids				
S0026	Stromal cell TF274	stromal cell	Bone marrow	Cell Line		Uni-ZAP XR
S0027	Smooth muscle, serum treated	Smooth muscle	Pulmana ry artery	Cell Line		Uni-ZAP XR
S0028	Smooth muscle, control	Smooth muscle	Pulmana ry artery	Cell Line		Uni-ZAP XR
S0029	brain stem	Brain stem	brain			Uni-ZAP XR
S0030	Brain pons	Brain Pons	Brain			Uni-ZAP XR
S0031	Spinal cord	Spinal cord	spinal cord			Uni-ZAP XR
S0032	Smooth muscle-ILb induced	Smooth muscle	Pulmana ry artery	Cell Line		Uni-ZAP XR
S0035	Brain medulla oblongata	Brain medulla oblongata	Brain			Uni-ZAP XR
S0036	Human Substantia Nigra	Human Substantia Nigra				Uni-ZAP XR
S0037	Smooth muscle, IL1b induced	Smooth muscle	Pulmana ry artery	Cell Line		Uni-ZAP XR
S0038	Human Whole Brain #2 - Oligo dT > 1.5Kb	Human Whole Brain #2				ZAP Express
S0039	Hypothalamus	Hypothalamus	Brain			Uni-ZAP XR
S0040	Adipocytes	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0042	Testes	Human Testes				ZAP Express
S0044	Prostate BPH	prostate BPH	Prostate		disease	Uni-ZAP XR
S0045	Endothelial cells- control	Endothelial cell	endothel ial cell- lung	Cell Line		Uni-ZAP XR
S0046	Endothelial-induced	Endothelial cell	endothel ial cell- lung	Cell Line		Uni-ZAP XR

S0048	Human Hypothalamus, Alzheimer's	Human Hypothalamus, Alzheimer's			disease	Uni-ZAP XR
S0049	Human Brain, Striatum	Human Brain, Striatum				Uni-ZAP XR
S0050	Human Frontal Cortex, Schizophrenia	Human Frontal Cortex, Schizophrenia			disease	Uni-ZAP XR
S0051	Human Hypothalamus, Schizophrenia	Human Hypothalamus, Schizophrenia			disease	Uni-ZAP XR
S0052	neutrophils control	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0053	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0106	STRIATUM DEPRESSION		BRAIN		disease	Uni-ZAP XR
S0110	Brain Amygdala Depression		Brain		disease	Uni-ZAP XR
S0112	Hypothalamus		Brain			Uni-ZAP XR
S0114	Anergic T-cell	Anergic T-cell		Cell Line		Uni-ZAP XR
S0116	Bone marrow	Bone marrow	Bone marrow			Uni-ZAP XR
S0118	Smooth muscle control 2	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0122	Osteoclastoma-normalized A	Osteoclastoma	bone		disease	pBluescript
S0124	Smooth muscle-edited A	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0126	Osteoblasts	Osteoblasts	Knee	Cell Line		Uni-ZAP XR
S0132	Epithelial-TNF $\alpha$ and INF induced	Airway Epithelial				Uni-ZAP XR
S0134	Apoptotic T-cell	apoptotic cells		Cell Line		Uni-ZAP XR
S0136	PERM TF274	stromal cell	Bone marrow	Cell Line		Lambda ZAP II
S0140	eosinophil-IL5 induced	eosinophil	lung	Cell Line		Uni-ZAP XR
S0142	Macrophage-oxLDL	macrophage-oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0144	Macrophage (GM-CSF treated)	Macrophage (GM-CSF treated)				Uni-ZAP XR
S0146	prostate-edited	prostate BPH	Prostate			Uni-ZAP XR
S0148	Normal Prostate	Prostate	prostate			Uni-ZAP XR
S0150	LNCAP prostate cell line	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
S0152	PC3 Prostate cell line	PC3 prostate cell line				Uni-ZAP XR
S0168	Prostate/LNCAP, subtraction I	PC3 prostate cell line				pBluescript
S0174	Prostate-BPH subtracted II	Human Prostate BPH				pBluescript
S0176	Prostate, normal, subtraction I	Prostate	prostate			Uni-ZAP XR
S0180	Bone Marrow Stroma, TNF&LPS ind	Bone Marrow Stroma, TNF & LPS induced			disease	Uni-ZAP XR
S0182	Human B Cell 8866	Human B- Cell 8866				Uni-ZAP XR
S0188	Prostate,BPH, Lib 2	Human Prostate BPH			disease	pSport1
S0190	Prostate BPH,Lib 2,	Human Prostate				pSport1



	subtracted	BPH				
S0192	Synovial Fibroblasts (control)	Synovial Fibroblasts				pSport1
S0194	Synovial hypoxia	Synovial Fibroblasts				pSport1
S0196	Synovial IL-1/TNF stimulated	Synovial Fibroblasts				pSport1
S0206	Smooth Muscle-HASTE normalized	Smooth muscle	Pulmonary artery	Cell Line		pBluescript
S0208	Mesangial cell, frac 1	Mesangial cell				pSport1
S0210	Mesangial cell, frac 2	Mesangial cell				pSport1
S0212	Bone Marrow Stromal Cell, untreated	Bone Marrow Stromal Cell, untreated				pSport1
S0214	Human Osteoclastoma, re-excision	Osteoclastoma	bone		disease	Uni-ZAP XR
S0216	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0218	Apoptotic T-cell, re-excision	apoptotic cells		Cell Line		Uni-ZAP XR
S0220	H. hypothalamus, frac A; re-excision	Hypothalamus	Brain			ZAP Express
S0222	H. Frontal cortex, epileptic; re-excision	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S0240	PYGD	PYGD				PCR II
S0242	Synovial Fibroblasts (III/TNF), sub	Synovial Fibroblasts				pSport1
S0250	Human Osteoblasts II	Human Osteoblasts	Femur		disease	pCMVSport 2.0
S0256	7TM-PHMIX	PBLS, 7TM receptor enriched				PCR II
S0258	7TM-PNMIX	PBLS, 7TM receptor enriched				PCR II
S0260	Spinal Cord, re-excision	Spinal cord	spinal cord			Uni-ZAP XR
S0262	PYCS	Human Antrum (PY CS)				PCR II
S0270	PTMIX	PTMIX (Human Thymus)	Thymus			PCR II
S0276	Synovial hypoxia-RSF subtracted	Synovial fibroblasts (rheumatoid)	Synovial tissue			pSport1
S0278	H Macrophage (GM-CSF treated), re-excision	Macrophage (GM-CSF treated)				Uni-ZAP XR
S0280	Human Adipose Tissue, re-excision	Human Adipose Tissue				Uni-ZAP XR
S0282	Brain Frontal Cortex, re-excision	Brain frontal cortex	Brain			Lambda ZAP II
S0290	H7TMCTB (Brain)	7TMCTB (Brain)	Kidney			PCR II
S0292	Osteoarthritis (OA-4)	Human Osteoarthritic Cartilage	Bone		disease	pSport1
S0294	Larynx tumor	Larynx tumor	Larynx, vocal cord		disease	pSport1
S0296	Normal lung	Normal lung	Lung			pSport1
S0298	Bone marrow stroma, treated	Bone marrow stroma, treated SB	Bone marrow			pSport1
S0300	Frontal	Frontal Lobe	Brain			Uni-ZAP XR

	lobe,dementia;re-excision	dementia/Alzheimer's				
S0306	Larynx normal #10 261-273	Larynx normal				pSport1
S0308	Spleen/normal	Spleen normal				pSport1
S0310	Normal trachea	Normal trachea				pSport1
S0312	Human osteoarthritic;fraction II	Human osteoarthritic cartilage			disease	pSport1
S0314	Human osteoarthritis;fraction I	Human osteoarthritic cartilage			disease	pSport1
S0316	Human Normal Cartilage,Fraction I	Human Normal Cartilage				pSport1
S0318	Human Normal Cartilage Fraction II	Human Normal Cartilage				pSport1
S0320	Human Larynx	Larynx	Epiglottis			pSport1
S0322	Siebben Polyposis	Siebben Polyposis				pSport1
S0324	Human Brain	Brain	Cerebellum			pSport1
S0326	Mammary Gland	Mammary Gland	Whole mammary gland			pSport1
S0328	Palate carcinoma	Palate carcinoma	Uvula		disease	pSport1
S0330	Palate normal	Palate normal	Uvula			pSport1
S0332	Pharynx carcinoma	Pharynx carcinoma	Hypopharynx			pSport1
S0334	Human Normal Cartilage Fraction III	Human Normal Cartilage				pSport1
S0336	Human Normal Cartilage Fraction IV	Human Normal Cartilage				pSport1
S0338	Human Osteoarthritic Cartilage Fraction III	Human osteoarthritic cartilage			disease	pSport1
S0340	Human Osteoarthritic Cartilage Fraction IV	Human osteoarthritic cartilage			disease	pSport1
S0342	Adipocytes;re-excision	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0344	Macrophage-oxLDL; re-excision	macrophage-oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0346	Human Amygdala;re-excision	Amygdala				Uni-ZAP XR
S0348	Cheek Carcinoma	Cheek Carcinoma			disease	pSport1
S0350	Pharynx Carcinoma	Pharynx carcinoma	Hypopharynx		disease	pSport1
S0352	Larynx Carcinoma	Larynx carcinoma			disease	pSport1
S0354	Colon Normal II	Colon Normal	Colon			pSport1
S0356	Colon Carcinoma	Colon Carcinoma	Colon		disease	pSport1
S0358	Colon Normal III	Colon Normal	Colon			pSport1
S0360	Colon Tumor II	Colon Tumor	Colon		disease	pSport1
S0362	Human Gastrocnemius	Gastrocnemius muscle				pSport1
S0364	Human Quadriceps	Quadriceps muscle				pSport1
S0366	Human Soleus	Soleus Muscle				pSport1
S0368	Human Pancreatic Langerhans	Islets of Langerhans				pSport1

S0370	Larynx carcinoma II	Larynx carcinoma			disease	pSport1
S0372	Larynx carcinoma III	Larynx carcinoma			disease	pSport1
S0374	Normal colon	Normal colon				pSport1
S0376	Colon Tumor	Colon Tumor			disease	pSport1
S0378	Pancreas normal PCA4 No	Pancreas Normal PCA4 No				pSport1
S0380	Pancreas Tumor PCA4 Tu	Pancreas Tumor PCA4 Tu			disease	pSport1
S0382	Larynx carcinoma IV	Larynx carcinoma			disease	pSport1
S0384	Tongue carcinoma	Tongue carcinoma			disease	pSport1
S0386	Human Whole Brain; re-excision	Whole brain	Brain			ZAP Express
S0388	Human Hypothalamus, schizophrenia, re-excision	Human Hypothalamus, Schizophrenia			disease	Uni-ZAP XR
S0390	Smooth muscle, control; re-excision	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0392	Salivary Gland	Salivary gland; normal				pSport1
S0394	Stomach; normal	Stomach; normal				pSport1
S0396	Uterus; normal	Uterus; normal				pSport1
S0398	Testis; normal	Testis; normal				pSport1
S0400	Brain; normal	Brain; normal				pSport1
S0402	Adrenal Gland, normal	Adrenal gland; normal				pSport1
S0404	Rectum normal	Rectum, normal				pSport1
S0406	Rectum tumour	Rectum tumour				pSport1
S0408	Colon, normal	Colon, normal				pSport1
S0410	Colon, tumour	Colon, tumour				pSport1
S0412	Temporal cortex-Alzheimer; subtracted	Temporal cortex, alzheimer			disease	Other
S0414	Hippocampus, Alzheimer Subtracted	Hippocampus, Alzheimer Subtracted				Other
S0418	CHME Cell Line; treated 5 hrs	CHME Cell Line; treated				pCMVSPORT 3.0
S0420	CHME Cell Line, untreated	CHME Cell line, untreated				pSport1
S0422	Mo7e Cell Line GM-CSF treated (1ng/ml)	Mo7e Cell Line GM-CSF treated (1ng/ml)				pCMVSPORT 3.0
S0424	TF-1 Cell Line GM-CSF Treated	TF-1 Cell Line GM-CSF Treated				pSport1
S0426	Monocyte activated; re-excision	Monocyte-activated	blood	Cell Line		Uni-ZAP XR
S0428	Neutrophils control; re-excision	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0430	Aryepiglottis Normal	Aryepiglottis Normal				pSport1
S0432	Sinus piniformis Tumour	Sinus piniformis Tumour				pSport1
S0434	Stomach Normal	Stomach Normal			disease	pSport1
S0436	Stomach Tumour	Stomach Tumour			disease	pSport1
S0438	Liver Normal Met5No	Liver Normal Met5No				pSport1
S0440	Liver Tumour Met 5 Tu	Liver Tumour				pSport1
S0442	Colon Normal	Colon Normal				pSport1
S0444	Colon Tumor	Colon Tumour			disease	pSport1

S0446	Tongue Tumour	Tongue Tumour				pSport1
S0448	Larynx Normal	Larynx Normal				pSport1
S0450	Larynx Tumour	Larynx Tumour				pSport1
S0452	Thymus	Thymus				pSport1
S0454	Placenta	Placenta	Placenta			pSport1
S0456	Tongue Normal	Tongue Normal				pSport1
S0458	Thyroid Normal (SDCA2 No)	Thyroid normal				pSport1
S0460	Thyroid Tumour	Thyroid Tumour				pSport1
S0462	Thyroid Thyroiditis	Thyroid Thyroiditis				pSport1
S0464	Larynx Normal	Larynx Normal				pSport1
S0466	Larynx Tumor	Larynx Tumor			disease	pSport1
S0468	Ea.hy.926 cell line	Ea.hy.926 cell line				pSport1
S0470	Adenocarcinoma	PYFD			disease	pSport1
S0472	Lung Mesothelium	PYBT				pSport1
S0474	Human blood platelets	Platelets	Blood platelets			Other
S0665	Human Amygdala; re- excision	Amygdala				Uni-ZAP XR
S3012	Smooth Muscle Serum Treated, Norm	Smooth muscle	Pulmana ry artery	Cell Line		pBluescript
S3014	Smooth muscle, serum induced, re-exc	Smooth muscle	Pulmana ry artery	Cell Line		pBluescript
S3018	TH1 cells	TH1 cells				Uni-ZAP XR
S3020	TH2 cells	TH2 cells				Uni-ZAP XR
S6014	H. hypothalamus, frac A	Hypothalamus	Brain			ZAP Express
S6016	H. Frontal Cortex, Epileptic	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S6022	H. Adipose Tissue	Human Adipose Tissue				Uni-ZAP XR
S6024	Alzheimers, spongy change	Alzheimer's/Spongy change	Brain		disease	Uni-ZAP XR
S6026	Frontal Lobe, Dementia	Frontal Lobe dementia/Alzheimer' 's	Brain			Uni-ZAP XR
S6028	Human Manic Depression Tissue	Human Manic depression tissue	Brain		disease	Uni-ZAP XR
T0001	Human Brown Fat	Brown Fat				pBluescript SK-
T0002	Activated T-cells	Activated T-Cell, PBL fraction	Blood	Cell Line		pBluescript SK-
T0003	Human Fetal Lung	Human Fetal Lung				pBluescript SK-
T0004	Human White Fat	Human White Fat				pBluescript SK-
T0006	Human Pineal Gland	Human Pinneal Gland				pBluescript SK-
T0007	Colon Epithelium	Colon Epithelium				pBluescriptISK -
T0008	Colorectal Tumor	Colorectal Tumor			disease	pBluescript SK-
T0010	Human Infant Brain	Human Infant Brain				Other
T0023	Human Pancreatic Carcinoma	Human Pancreatic Carcinoma			disease	pBluescript SK-
T0027	Human Prostate Epithelium	Human Prostate Epithelium				pBluescript SK-
T0039	HSA 172 Cells	Human HSA172 cell line				pBluescript SK-

T0040	HSC172 cells	SA172 Cells				pBluescript SK-
T0041	Jurkat T-cell G1 phase	Jurkat T-cell				pBluescript SK-
T0042	Jurkat T-Cell, S phase	Jurkat T-Cell Line				pBluescript SK-
T0048	Human Aortic Endothelium	Human Aortic Endothelium				pBluescript SK-
T0049	Aorta endothelial cells + TNF- $\alpha$	Aorta endothelial cells				pBluescript SK-
T0060	Human White Adipose	Human White Fat				pBluescript SK-
T0067	Human Thyroid	Human Thyroid				pBluescript SK-
T0068	Normal Ovary, Premenopausal	Normal Ovary, Premenopausal				pBluescript SK-
T0069	Human Uterus, normal	Human Uterus, normal				pBluescript SK-
T0071	Human Bone Marrow	Human Bone Marrow				pBluescript SK-
T0078	Human Liver, normal adult	Human Liver, normal Adult				pBluescript SK-
T0079	Human Kidney, normal Adult	Human Kidney, normal Adult				pBluescript SK-
T0082	Human Adult Retina	Human Adult Retina				pBluescript SK-
T0086	Human Pancreatic Carcinoma — Screened	Human Pancreatic Carcinoma			disease	pBluescript SK-
T0087	Alzheimer's, exon trap, 712P				disease	pAMP
T0090	Liver, normal					pBluescript SK-
T0103	Human colon carcinoma (HCC) cell line					pBluescript SK-
T0104	HCC cell line metastasis to liver					pBluescript SK-
T0109	Human (HCC) cell line liver (mouse) metastasis, remake					pBluescript SK-
T0110	Human colon carcinoma (HCC) cell line, remake					pBluescript SK-
T0112	Human (Caco-2) cell line, adenocarcinoma, colon					pBluescript SK-
T0114	Human (Caco-2) cell line, adenocarcinoma, colon, remake					pBluescript SK-
T0115	Human Colon Carcinoma (HCC) cell line					pBluescript SK-
L0002	Atrium cDNA library Human heart					
L0005	Clontech human aorta polyA+ mRNA (#6572)					
L0010	GeneTrack, 4p16.3 JM Rommens					
L0021	Human adult					

	(K.Okubo)					
L0022	Human adult lung 3" directed MboI cDNA					
L0032	Human chromosome 12p cDNAs					
L0034	Human chromosome 14					
L0040	Human colon mucosa					
L0041	Human epidermal keratinocyte					
L0043	Human HaCaT keratinocyte cDNA					
L0044	Human K562 erythroleukemic cells					
L0052	Human normalized K562-cDNA					
L0053	Human pancreatic tumor					
L0055	Human promyelocyte					
L0060	Human thymus NSTH II					
L0065	Liver HepG2 cell line.					
L0070	Selected chromosome 21 cDNA library					
L0096	Subtracted human retina					
L0097	Subtracted human retinal pigment epithelium (RPE)					
L0103	DKFZphamy1	amygdala				
L0105	Human aorta polyA+ (TFujiwara)	aorta				
L0109	Human brain cDNA	brain				
L0118	Human fetal brain S. Meier-Ewert	brain				
L0140	Human pancreatic cancer (CWallrapp)	pancreatic cancer				
L0142	Human placenta cDNA (TFujiwara)	placenta				
L0143	Human placenta polyA+ (TFujiwara)	placenta				
L0149	DKFZphsnu1	subthalamic nucleus				
L0152	DKFZphthml	thymus				
L0157	Human fetal brain (TFujiwara)		brain			
L0158	Human fetal brain QBogin		brain			
L0163	Human heart cDNA (YNakamura)		heart			
L0171	Human lung adenocarcinoma A549	lung adenocarcinoma		A549		
L0181	HeLa cDNA (T.Noma)			HeLa		
L0185	Human immortalized fibroblasts (H.L.Ozer)			HS74 and its SV40-transformed sublines		
L0194	Human pancreatic cancer cell line Patu	pancreatic cancer		Patu 8988t		

	8988t					
L0309	Human E8CASS	breast adenocarcinoma		E8CASS; variant of MCF7		
L0351	Infant brain, Bento Soares					BA, M13-derived
L0352	Normalized infant brain, Bento Soares					BA, M13-derived
L0353	21q Placenta, F. Tassone and K. Gardiner					Bluescript
L0354	JG, Human foetal Kidney tissue					Bluescript
L0355	P, Human foetal Brain Whole tissue					Bluescript
L0356	S, Human foetal Adrenals tissue					Bluescript
L0360	Y, Human Placenta tissue					Bluescript KS II+
L0361	Stratagene ovary (#937217)		ovary			Bluescript SK-
L0362	Stratagene ovarian cancer (#937219)					Bluescript SK-
L0363	NCI CGAP GC2	germ cell tumor				Bluescript SK-
L0364	NCI CGAP GC5	germ cell tumor				Bluescript SK-
L0365	NCI CGAP Phe1	pheochromocytoma				Bluescript SK-
L0366	Stratagene schizo brain S11	schizophrenic brain S-11 frontal lobe				Bluescript SK-
L0367	NCI CGAP Sch1	Schwannoma tumor				Bluescript SK-
L0368	NCI CGAP SS1	synovial sarcoma				Bluescript SK-
L0369	NCI CGAP_AA1	adrenal adenoma	adrenal gland			Bluescript SK-
L0370	Johnston frontal cortex	pooled frontal lobe	brain			Bluescript SK-
L0371	NCI CGAP Br3	breast tumor	breast			Bluescript SK-
L0372	NCI CGAP Co12	colon tumor	colon			Bluescript SK-
L0373	NCI CGAP Co11	tumor	colon			Bluescript SK-
L0374	NCI CGAP Co2	tumor	colon			Bluescript SK-
L0375	NCI CGAP Kid6	kidney tumor	kidney			Bluescript SK-
L0376	NCI CGAP Lar1	larynx	larynx			Bluescript SK-
L0378	NCI CGAP Lu1	lung tumor	lung			Bluescript SK-
L0379	NCI CGAP_Lym3	lymphoma	lymph node			Bluescript SK-
L0381	NCI CGAP_HN4	squamous cell carcinoma	pharynx			Bluescript SK-
L0382	NCI CGAP Pr25	epithelium (cell line)	prostate			Bluescript SK-
L0383	NCI CGAP_Pr24	invasive tumor (cell line)	prostate			Bluescript SK-
L0384	NCI CGAP Pr23	prostate tumor	prostate			Bluescript SK-
L0385	NCI CGAP Gas1	gastric tumor	stomach			Bluescript SK-
L0386	NCI CGAP_HN3	squamous cell carcinoma from base of tongue	tongue			Bluescript SK-
L0387	NCI CGAP_GCB0	germinal center B-cells	tonsil			Bluescript SK-
L0388	NCI CGAP_HN6	normal gingiva (cell line from immortalized kerati				Bluescript SK-
L0389	NCI CGAP_HN5	normal gingiva (cell line from primary				Bluescript SK-

		keratinocyt				
L0393	B, Human Liver tissue					gt11
L0394	H, Human adult Brain Cortex tissue					gt11
L0411	1-NIB					Lafmid BA
L0414	b4HB3MA					Lafmid BA
L0415	b4HB3MA Cot8-HAP- Ft					Lafmid BA
L0417	b4HB3MA-Cot0.38- HAP-Ft-6					Lafmid BA
L0418	b4HB3MA- Cot109+10-Bio					Lafmid BA
L0420	b4HB3MA- Cot109+103-Bio					Lafmid BA
L0422	b4HB3MA-Cot12- HAP-B					Lafmid BA
L0423	b4HB3MA-Cot12- HAP-Ft					Lafmid BA
L0426	b4HB3MA-Cot51.5- HAP-Ft					Lafmid BA
L0427	b4HB3MA-FT20%- Biotin					Lafmid BA
L0430	Cot250Ft-b4HB3MA					Lafmid BA
L0434	Infant brain library of Dr. M. Soares					lafmid BA
L0435	Infant brain, LLNL array of Dr. M. Soares 1NIB					lafmid BA
L0437	N-b4HB3MA-Cot109					Lafmid BA
L0438	normalized infant brain cDNA	total brain	brain			lafmid BA
L0439	Soares infant brain 1NIB		whole brain			Lafmid BA
L0440	1HB3MK					Lafmid BK
L0442	4HB3MK					Lafmid BK
L0443	b4HB3MK					Lafmid BK
L0444	HB3MK					Lafmid BK
L0448	3HFLSK20					Lafmid K
L0451	N3HFLSK20					Lafmid K
L0455	Human retina cDNA randomly primed sublibrary	retina	eye			lambda gt10
L0456	Human retina cDNA Tsp509I-cleaved sublibrary	retina	eye			lambda gt10
L0459	Adult heart, Clontech					Lambda gt11
L0460	Adult heart, Lambda gt11					Lambda gt11
L0462	WATM1					lambda gt11
L0465	TEST1, Human adult Testis tissue					lambda nm1149
L0468	HE6W					lambda zap
L0469	T, Human adult Rhabdomyosarcoma cell-line					Lambda Zap
L0470	BL29 Burkitt's lymphoma, Pascalis Sideras					lambda ZAP 2
L0471	Human fetal heart,					Lambda ZAP



	Lambda ZAP Express					Express
L0475	KG1-a Lambda Zap Express cDNA library			KG1-a		Lambda Zap Express (Stratagene)
L0476	Fetal brain, Stratagene					Lambda ZAP II
L0477	HPLA CCLee	placenta				Lambda ZAP II
L0480	Stratagene cat#937212 (1992)					Lambda ZAP, pBluescript SK(-)
L0481	CD34+DIRECTIONAL					Lambda ZAPII
L0483	Human pancreatic islet					Lambda ZAPII
L0485	STRATAGENE Human skeletal muscle cDNA library, cat. #936215.	skeletal muscle	leg muscle			Lambda ZAPII
L0493	NCI_CGAP_Ov26	papillary serous carcinoma	ovary			pAMP1
L0497	NCI_CGAP_HSC4	CD34+, CD38- from normal bone marrow donor	bone marrow			pAMP1
L0498	NCI_CGAP_HSC3	CD34+, T negative, patient with chronic myelogenous	bone marrow			pAMP1
L0499	NCI_CGAP_HSC2	stem cell 34+/38+	bone marrow			pAMP1
L0500	NCI CGAP Brn20	oligodendroglioma	brain			pAMP1
L0501	NCI CGAP Brn21	oligodendroglioma	brain			pAMP1
L0502	NCI CGAP Br15	adenocarcinoma	breast			pAMP1
L0503	NCI CGAP Br17	adenocarcinoma	breast			pAMP1
L0504	NCI_CGAP_Br13	breast carcinoma in situ	breast			pAMP1
L0505	NCI CGAP Br12	invasive carcinoma	breast			pAMP1
L0506	NCI_CGAP_Br16	lobular carcinoma in situ	breast			pAMP1
L0507	NCI CGAP Br14	normal epithelium	breast			pAMP1
L0508	NCI_CGAP_Lu25	bronchioalveolar carcinoma	lung			pAMP1
L0509	NCI_CGAP_Lu26	invasive adenocarcinoma	lung			pAMP1
L0510	NCI_CGAP_Ov33	borderline ovarian carcinoma	ovary			pAMP1
L0511	NCI_CGAP_Ov34	borderline ovarian carcinoma	ovary			pAMP1
L0512	NCI_CGAP_Ov36	borderline ovarian carcinoma	ovary			pAMP1
L0513	NCI_CGAP_Ov37	early stage papillary serous carcinoma	ovary			pAMP1
L0514	NCI_CGAP_Ov31	papillary serous carcinoma	ovary			pAMP1
L0515	NCI_CGAP_Ov32	papillary serous carcinoma	ovary			pAMP1
L0517	NCI CGAP Pr1					pAMP10
L0518	NCI CGAP Pr2					pAMP10
L0519	NCI CGAP Pr3					pAMP10
L0520	NCI_CGAP_Alv1	alveolar rhabdomyosarcoma				pAMP10

L0521	NCI CGAP Ew1	Ewing's sarcoma				pAMP10
L0522	NCI CGAP Kid1	kidney				pAMP10
L0523	NCI CGAP Lip2	liposarcoma				pAMP10
L0524	NCI CGAP Li1	liver				pAMP10
L0525	NCI CGAP Li2	liver				pAMP10
L0526	NCI CGAP_Pr12	metastatic prostate bone lesion				pAMP10
L0527	NCI CGAP Ov2	ovary				pAMP10
L0528	NCI CGAP Pr5	prostate				pAMP10
L0529	NCI CGAP Pr6	prostate				pAMP10
L0530	NCI CGAP Pr8	prostate				pAMP10
L0532	NCI CGAP Thy1	thyroid				pAMP10
L0533	NCI CGAP_HSC1	stem cells	bone marrow			pAMP10
L0534	Chromosome 7 Fetal Brain cDNA Library	brain	brain			pAMP10
L0535	NCI CGAP_Br5	infiltrating ductal carcinoma	breast			pAMP10
L0536	NCI CGAP Br4	normal ductal tissue	breast			pAMP10
L0537	NCI CGAP_Ov6	normal cortical stroma	ovary			pAMP10
L0538	NCI CGAP_Ov5	normal surface epithelium	ovary			pAMP10
L0539	Chromosome 7 Placental cDNA Library		placenta			pAMP10
L0540	NCI CGAP_Pr10	invasive prostate tumor	prostate			pAMP10
L0541	NCI CGAP_Pr7	low-grade prostatic neoplasia	prostate			pAMP10
L0542	NCI CGAP_Pr11	normal prostatic epithelial cells	prostate			pAMP10
L0543	NCI CGAP_Pr9	normal prostatic epithelial cells	prostate			pAMP10
L0544	NCI CGAP_Pr4	prostatic intraepithelial neoplasia - high grade	prostate			pAMP10
L0545	NCI CGAP_Pr4.1	prostatic intraepithelial neoplasia - high grade	prostate			pAMP10
L0546	NCI CGAP_Pr18	stroma	prostate			pAMP10
L0547	NCI CGAP_Pr16	tumor	prostate			pAMP10
L0549	NCI CGAP_HN10	carcinoma in situ from retromolar trigone				pAMP10
L0550	NCI CGAP_HN9	normal squamous epithelium from retromolar trigone				pAMP10
L0551	NCI CGAP_HN7	normal squamous epithelium, floor of mouth				pAMP10
L0552	NCI CGAP_HN8	well-differentiated invasive carcinoma, floor of m				pAMP10
L0553	NCI CGAP_Co22	colonic adenocarcinoma	colon			pAMP10
L0554	NCI CGAP Li8		liver			pAMP10

L0555	NCI CGAP Lu34	large cell carcinoma	lung			pAMP10
L0556	NCI CGAP Lu34.1	large cell carcinoma	lung			pAMP10
L0558	NCI CGAP_Ov40	endometrioid ovarian metastasis	ovary			pAMP10
L0559	NCI CGAP_Ov39	papillary serous ovarian metastasis	ovary			pAMP10
L0560	NCI CGAP_HN12	moderate to poorly differentiated invasive carcino	tongue			pAMP10
L0561	NCI CGAP_HN11	normal squamous epithelium	tongue			pAMP10
L0562	Chromosome 7 HeLa cDNA Library			HeLa cell line; ATCC		pAMP10
L0563	Human Bone Marrow Stromal Fibroblast	bone marrow				pBluescript
L0564	Jia bone marrow stroma	bone marrow stroma				pBluescript
L0565	Normal Human Trabecular Bone Cells	Bone	Hip			pBluescript
L0579	Human fetal brain QBoqin2	cerebrum and cerebellum				pBluescript SK
L0581	Stratagene liver (#937224)		liver			pBluescript SK
L0584	Stratagene cDNA library Human heart, cat#936208					pBluescript SK(+)
L0586	HTCDL1					pBluescript SK(-)
L0587	Stratagene colon HT29 (#937221)					pBluescript SK-
L0588	Stratagene endothelial cell 937223					pBluescript SK-
L0589	Stratagene fetal retina 937202					pBluescript SK-
L0590	Stratagene fibroblast (#937212)					pBluescript SK-
L0591	Stratagene HeLa cell s3 937216					pBluescript SK-
L0592	Stratagene hNT neuron (#937233)					pBluescript SK-
L0593	Stratagene neuroepithelium (#937231)					pBluescript SK-
L0594	Stratagene neuroepithelium NT2RAMI 937234					pBluescript SK-
L0595	Stratagene NT2 neuronal precursor 937230	neuroepithelial cells	brain			pBluescript SK-
L0596	Stratagene colon (#937204)		colon			pBluescript SK-
L0597	Stratagene corneal stroma (#937222)		cornea			pBluescript SK-
L0598	Morton Fetal Cochlea	cochlea	ear			pBluescript SK-
L0599	Stratagene lung (#937210)		lung			pBluescript SK-
L0600	Weizmann Olfactory	olfactory epithelium	nose			pBluescript

	Epithelium					SK-
L0601	Stratagene pancreas (#937208)		pancreas			pBluescript SK-
L0602	Pancreatic Islet	pancreatic islet	pancreas			pBluescript SK-
L0603	Stratagene placenta (#937225)		placenta			pBluescript SK-
L0604	Stratagene muscle 937209	muscle	skeletal muscle			pBluescript SK-
L0605	Stratagene fetal spleen (#937205)	fetal spleen	spleen			pBluescript SK-
L0606	NCI_CGAP_Lym5	follicular lymphoma	lymph node			pBluescript SK-
L0607	NCI_CGAP_Lym6	mantle cell lymphoma	lymph node			pBluescript SK-
L0608	Stratagene lung carcinoma 937218	lung carcinoma	lung	NCI-H69		pBluescript SK-
L0609	Schiller astrocytoma	astrocytoma	brain			pBluescript SK- (Stratagene)
L0611	Schiller meningioma	meningioma	brain			pBluescript SK- (Stratagene)
L0612	Schiller oligodendroglioma	oligodendroglioma	brain			pBluescript SK- (Stratagene)
L0615	22 week old human fetal liver cDNA library					pBluescriptII SK(-)
L0616	Chromosome 21 exon					pBluescriptIIK S+
L0622	HM1					pcDNAII (Invitrogen)
L0623	HM3	pectoral muscle (after mastectomy)				pcDNAII (Invitrogen)
L0625	NCI_CGAP_AR1	bulk alveolar tumor				pCMV-SPORT2
L0626	NCI_CGAP_GC1	bulk germ cell seminoma				pCMV-SPORT2
L0627	NCI_CGAP_Co1	bulk tumor	colon			pCMV-SPORT2
L0628	NCI_CGAP_Ov1	ovary bulk tumor	ovary			pCMV-SPORT2
L0629	NCI_CGAP_Mel3	metastatic melanoma to bowel	bowel (skin primary)			pCMV-SPORT4
L0630	NCI_CGAP_CNS1	substantia nigra	brain			pCMV-SPORT4
L0631	NCI_CGAP_Br7		breast			pCMV-SPORT4
L0632	NCI_CGAP_Li5	hepatic adenoma	liver			pCMV-SPORT4
L0633	NCI_CGAP_Lu6	small cell carcinoma	lung			pCMV-SPORT4
L0634	NCI_CGAP_Ov8	serous adenocarcinoma	ovary			pCMV-SPORT4
L0635	NCI_CGAP_PNS1	dorsal root ganglion	peripheral nervous system			pCMV-SPORT4

L0636	NCI_CGAP_Pit1	four pooled pituitary adenomas	brain			pCMV-SPORT6
L0637	NCI_CGAP_Brn53	three pooled meningiomas	brain			pCMV-SPORT6
L0638	NCI_CGAP_Brn35	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0639	NCI_CGAP_Brn52	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0640	NCI_CGAP_Br18	four pooled high-grade tumors, including two prima	breast			pCMV-SPORT6
L0641	NCI_CGAP_Co17	juvenile granulosa tumor	colon			pCMV-SPORT6
L0642	NCI_CGAP_Co18	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0643	NCI_CGAP_Co19	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0644	NCI_CGAP_Co20	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0645	NCI_CGAP_Co21	moderately differentiated adenocarcinoma	colon			pCMV-SPORT6
L0646	NCI_CGAP_Co14	moderately-differentiated adenocarcinoma	colon			pCMV-SPORT6
L0647	NCI_CGAP_Sar4	five pooled sarcomas, including myxoid liposarcoma	connective tissue			pCMV-SPORT6
L0648	NCI_CGAP_Eso2	squamous cell carcinoma	esophagus			pCMV-SPORT6
L0649	NCI_CGAP_GUI1	2 pooled high-grade transitional cell tumors	genitourinary tract			pCMV-SPORT6
L0650	NCI_CGAP_Kid13	2 pooled Wilms' tumors, one primary and one metast	kidney			pCMV-SPORT6
L0651	NCI_CGAP_Kid8	renal cell tumor	kidney			pCMV-SPORT6
L0652	NCI_CGAP_Lu27	four pooled poorly-differentiated adenocarcinomas	lung			pCMV-SPORT6
L0653	NCI_CGAP_Lu28	two pooled squamous cell carcinomas	lung			pCMV-SPORT6
L0654	NCI_CGAP_Lu31		lung, cell line			pCMV-SPORT6
L0655	NCI_CGAP_Lym12	lymphoma, follicular mixed small and large cell	lymph node			pCMV-SPORT6
L0656	NCI_CGAP_Ov38	normal epithelium	ovary			pCMV-SPORT6
L0657	NCI_CGAP_Ov23	tumor, 5 pooled (see description)	ovary			pCMV-SPORT6
L0658	NCI_CGAP_Ov35	tumor, 5 pooled (see description)	ovary			pCMV-SPORT6
L0659	NCI_CGAP_Pan1	adenocarcinoma	pancreas			pCMV-SPORT6

L0661	NCI_CGAP_Mel15	malignant melanoma, metastatic to lymph node	skin			pCMV-SPORT6
L0662	NCI_CGAP_Gas4	poorly differentiated adenocarcinoma with signet r	stomach			pCMV-SPORT6
L0663	NCI_CGAP_Ut2	moderately-differentiated endometrial adenocarcinoma	uterus			pCMV-SPORT6
L0664	NCI_CGAP_Ut3	poorly-differentiated endometrial adenocarcinoma,	uterus			pCMV-SPORT6
L0665	NCI_CGAP_Ut4	serous papillary carcinoma, high grade, 2 pooled t	uterus			pCMV-SPORT6
L0666	NCI_CGAP_Ut1	well-differentiated endometrial adenocarcinoma, 7	uterus			pCMV-SPORT6
L0667	NCI_CGAP_CML1	myeloid cells, 18 pooled CML cases, BCR/ABL rearra	whole blood			pCMV-SPORT6
L0669	Human MCF7 cDNA subtracted with MDA-MB-231 cDNA	breast adenocarcinoma	breast	MCF7		pCR II [Invitrogen]
L0681	Stanley Frontal SN individual	frontal lobe (see description)	brain			pCR2.1 (Invitrogen)
L0682	Stanley Frontal NB pool 2	frontal lobe (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0683	Stanley Frontal NS pool 2	frontal lobe (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0684	Stanley Frontal SB pool 1	frontal lobe (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0686	Stanley Frontal SN pool 2	frontal lobe (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0687	Stanley Hippocampus NB pool 1	hippocampus (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0689	Stanley Hippocampus SN pool 1	hippocampus (see description)	brain			pCR2.1-TOPO (Invitrogen)
L0695	Human Glioblastoma Cell		Brain	BT-325		PCR II, Invitrogen
L0697	Testis 1					PGEM 5zf(+)
L0698	Testis 2					PGEM 5zf(+)
L0717	Gessler Wilms tumor					pSPORT1
L0718	Testis 5					pSPORT1
L0731	Soares_pregnant_uterus NbHPU		uterus			pT7T3-Pac
L0738	Human colorectal cancer					pT7T3D
L0739	Soares placenta Nb2HP-B					pT7T3D (Pharmacia) with a modified polylinker
L0740	Soares melanocyte 2NbHM	melanocyte				pT7T3D (Pharmacia) with a modified polylinker

L0741	Soares adult brain N2b4HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0742	Soares adult brain N2b5HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0743	Soares breast 2NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker
L0744	Soares breast 3NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker
L0745	Soares retina N2b4HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0746	Soares retina N2b5HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0747	Soares fetal heart_Nb HH19W		heart			pT7T3D (Pharmacia) with a modified polylinker
L0748	Soares fetal liver spleen 1NFLS		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0749	Soares fetal liver_sple en_1NFLS_S1		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0750	Soares fetal_lung_Nb HL19W		lung			pT7T3D (Pharmacia) with a modified polylinker
L0751	Soares ovary tumor NbHOT	ovarian tumor	ovary			pT7T3D (Pharmacia) with a modified polylinker
L0752	Soares parathyroid_tu mor_NbHPA	parathyroid tumor	parathyr oid gland			pT7T3D (Pharmacia) with a modified polylinker
L0753	Soares pineal gland		pineal			pT7T3D

	N3HPG		gland			(Pharmacia) with a modified polylinker
L0754	Soares placenta Nb2HP		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0755	Soares_placenta_8to9w eeks_2NbHP8to9W		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0756	Soares_multiple_sclero sis_2NbHMSP	multiple sclerosis lesions				pT7T3D (Pharmacia) with a modified polylinker V TYPE
L0757	Soares_senescent_fibro blasts_NbHSF	senescent fibroblast				pT7T3D (Pharmacia) with a modified polylinker V TYPE
L0758	Soares_testis_NHT					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0759	Soares_total_fetus_Nb 2HF8_9w					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0760	Barstead aorta HPLRB3	aorta				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0761	NCI_CGAP_CLL1	B-cell, chronic lymphocytic leukemia				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0762	NCI_CGAP_Br1.1	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0763	NCI_CGAP_Br2	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0764	NCI_CGAP_Co3	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker



L0765	NCI_CGAP_Co4	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0766	NCI_CGAP_GCB1	germinal center B cell				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0767	NCI_CGAP_GC3	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0768	NCI_CGAP_GC4	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0769	NCI_CGAP_Bm25	anaplastic oligodendroglioma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0770	NCI_CGAP_Bm23	glioblastoma (pooled)	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0771	NCI_CGAP_Co8	adenocarcinoma	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0772	NCI_CGAP_Co10	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0773	NCI_CGAP_Co9	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0774	NCI_CGAP_Kid3		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0775	NCI_CGAP_Kid5	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0776	NCI_CGAP_Lu5	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0777	Soares NhHMPu S1	Pooled human	mixed			pT7T3D-Pac

		melanocyte, fetal heart, and pregnant	(see below)			(Pharmacia) with a modified polylinker
L0778	Barstead pancreas HPLRB1		pancreas			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0779	Soares_NFL_T_GBC_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0780	Soares_NSF_F8_9W_OT_PA_P_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0781	Barstead prostate BPH HPLRB4		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0782	NCI_CGAP_Pr21	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0783	NCI_CGAP_Pr22	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0784	NCI_CGAP_Lei2	leiomyosarcoma	soft tissue			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0785	Barstead spleen HPLRB2		spleen			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0786	Soares_NbHFB		whole brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0787	NCI_CGAP_Sub1					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0788	NCI_CGAP_Sub2					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0789	NCI_CGAP_Sub3					pT7T3D-Pac (Pharmacia)

						with a modified polylinker
L0790	NCI_CGAP_Sub4					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0791	NCI_CGAP_Sub5					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0792	NCI_CGAP_Sub6					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0793	NCI_CGAP_Sub7					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0794	NCI_CGAP_GC6	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0796	NCI_CGAP_Brn50	medulloblastoma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0800	NCI_CGAP_Co16	colon tumor, RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0803	NCI_CGAP_Kid11		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0804	NCI_CGAP_Kid12	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0805	NCI_CGAP_Lu24	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0806	NCI_CGAP_Lu19	squamous cell carcinoma, poorly differentiated (4	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0807	NCI_CGAP_Ov18	fibrotheoma	ovary			pT7T3D-Pac (Pharmacia) with a

						modified polylinker
L0808	Barstead prostate BPH HPLRB4 1		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0809	NCI CGAP_Pr28		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0811	BATM2					PTZ18
L2249	Human aortic endothelium	aortic endothelium				
L2250	Human cerebral cortex	cerebral cortex				
L2251	Human fetal lung	Fetal lung				
L2269	NCI CGAP Thy11	follicular carcinoma	thyroid			pAMP10
L3872	NCI CGAP_Skn1		skin, normal, 4 pooled sa			pCMV-SPORT6
L3904	NCI CGAP_Brn64	glioblastoma with EGFR amplification	brain			pCMV-SPORT6
L3905	NCI CGAP_Brn67	anaplastic oligodendroglioma with 1p/19q loss	brain			pCMV-SPORT6
L4497	NCI CGAP_Br22	invasive ductal carcinoma, 3 pooled samples	breast			pCMV-SPORT6
L4500	NCI CGAP_HN16	moderate to poorly differentiated invasive carcino	mouth			pAMP10
L4501	NCI CGAP_Sub8					pT7T3D-Pac (Pharmacia) with a modified polylinker
L4559	NCI CGAP_Thy3	follicular carcinoma	thyroid			pCMV-SPORT6
L4669	NCI CGAP_Ov41	serous papillary tumor	ovary			pCMV-SPORT6
L4747	NCI CGAP_Brn41	oligodendroglioma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L4775	NCI CGAP_Thy12	papillary carcinoma	thyroid			pAMP10
L5286	NCI CGAP_Thy10	medullary carcinoma	thyroid			pAMP10
L5564	NCI CGAP_HN20		normal head/neck tissue			pAMP1
L5565	NCI CGAP_Brn66	glioblastoma with probably TP53 mutation and witho	brain			pCMV-SPORT6
L5566	NCI CGAP_Brn70	anaplastic oligodendroglioma	brain			pCMV-SPORT6.ccd
L5568	NCI CGAP_HN21	nasopharyngeal carcinoma	head/neck			pAMP1

L5569	NCI_CGAP_HN17	normal epithelium	nasopharynx			pAMP10
L5574	NCI_CGAP_HN19	normal epithelium	nasopharynx			pAMP10
L5575	NCI_CGAP_Brn65	glioblastoma without EGFR amplification	brain			pCMV-SPORT6
L5622	NCI_CGAP_Skn3		skin			pCMV-SPORT6
L5623	NCI_CGAP_Skn4	squamous cell carcinoma	skin			pCMV-SPORT6

**TABLE 5**

OMIM Reference	Description
100650	Fetal alcohol syndrome
100650	Alcohol intolerance, acute
100678	ACAT2 deficiency
100690	Myasthenic syndrome, slow-channel congenital, 601462
100730	Myasthenia gravis, neonatal transient
102200	Somatotrophinoma
102578	Leukemia, acute promyelocytic, PML/RARA type
102770	Myoadenylate deaminase deficiency
102772	[AMP deaminase deficiency, erythrocytic]
103050	Autism, succinylpurinemic
103050	Adenylosuccinase deficiency
103581	Albright hereditary osteodystrophy-2
103950	Emphysema due to alpha-2-macroglobulin deficiency
104311	Alzheimer disease-3
104500	Amelogenesis imperfecta-2, hypoplastic local type
104770	Amyloidosis, secondary, susceptibility to
105580	Anal canal carcinoma
106100	Angioedema, hereditary
106150	Hypertension, essential, susceptibility to
106150	Preeclampsia, susceptibility to
106165	Hypertension, essential, 145500
106180	Myocardial infarction, susceptibility to
106210	Peters anomaly
106210	Cataract, congenital, with late-onset corneal dystrophy
106210	Foveal hypoplasia, isolated, 136520
106210	Aniridia
106300	Ankylosing spondylitis
107250	Anterior segment mesenchymal dysgenesis
107271	CD59 deficiency

107300	Antithrombin III deficiency
107470	Atypical mycobacterial infection, familial disseminated, 209950
107470	BCG infection, generalized familial
107470	Tuberculosis, susceptibility to
107670	Apolipoprotein A-II deficiency
107680	ApoA-I and apoC-III deficiency, combined
107680	Corneal clouding, autosomal recessive
107680	Amyloidosis, 3 or more types
107680	Hypertriglyceridemia, one form
107680	Hypoalphalipoproteinemia
107720	Hypertriglyceridemia
107730	Apolipoprotein B-100, ligand-defective
107730	Abetalipoproteinemia
107730	Hyperbetalipoproteinemia
107730	Hypobetalipoproteinemia
107741	Hyperlipoproteinemia, type III
107777	Diabetes insipidus, nephrogenic, autosomal recessive, 222000
107970	Arrhythmogenic right ventricular dysplasia-1
108725	Atherosclerosis, susceptibility to
108800	Atrial septal defect, secundum type
108985	Atrophia areata
109150	Machado-Joseph disease
109270	Renal tubular acidosis, distal, 179800
109270	Spherocytosis, hereditary
109270	[Acanthocytosis, one form]
109270	[Elliptocytosis, Malaysian-Melanesian type]
109270	Hemolytic anemia due to band 3 defect
109400	Basal cell nevus syndrome
109543	Leukemia, chronic lymphocytic, B-cell
109560	Leukemia/lymphoma, B-cell, 3
109565	Lymphoma, B-cell
109565	Lymphoma, diffuse large cell
109700	Hemodialysis-related amyloidosis
110100	Blepharophimosis, epicanthus inversus, and ptosis, type 1
110700	Vivax malaria, susceptibility to
112261	Fibrodysplasia ossificans progressiva
112262	Fibrodysplasia ossificans progressiva, 135100
112410	Hypertension with brachydactyly
113100	Brachydactyly, type C
113300	Brachydactyly type E
113705	Ovarian cancer
113705	Breast cancer-1
113721	Breast cancer
113900	Heart block, progressive familial, type I

114208	Malignant hyperthermia susceptibility 5, 601887
114208	Hypokalemic periodic paralysis, 170400
114290	Campomelic dysplasia with autosomal sex reversal
114550	Hepatocellular carcinoma
114835	Monocyte carboxyesterase deficiency
115500	Acatalasemia
115650	Cataract, anterior polar-1
115660	Cataract, cerulean, type 1
116600	Cataract, posterior polar
116806	Colorectal cancer
116860	Cavernous angiomatous malformations
117700	[Hypoceruloplasminemia, hereditary]
117700	Hemosiderosis, systemic, due to aceruloplasminemia
118210	Charcot-Marie-Tooth neuropathy-2A
118425	Myotonia congenita, dominant, 160800
118425	Myotonia congenita, recessive, 255700
118425	Myotonia levior, recessive
118470	[CETP deficiency]
118485	Polycystic ovary syndrome with hyperandrogenemia
118504	Epilepsy, benign neonatal, type 1, 121200
118504	Epilepsy, nocturnal frontal lobe, 600513
118800	Choreoathetosis, familial paroxysmal
119300	van der Woude syndrome
120070	Alport syndrome, autosomal recessive, 203780
120110	Metaphyseal chondrodysplasia, Schmid type
120120	Epidermolysis bullosa dystrophica, dominant, 131750
120120	Epidermolysis bullosa dystrophica, recessive, 226600
120120	Epidermolysis bullosa, pretibial, 131850
120131	Alport syndrome, autosomal recessive, 203780
120131	Hematuria, familial benign
120180	Ehlers-Danlos syndrome, type III
120180	Ehlers-Danlos syndrome, type IV, 130050
120180	Fibromuscular dysplasia of arteries, 135580
120180	Aneurysm, familial, 100070
120190	Ehlers-Danlos syndrome, type I, 130000
120220	Bethlem myopathy, 158810
120240	Bethlem myopathy, 158810
120250	Bethlem myopathy, 158810
120260	Epiphyseal dysplasia, multiple, type 2, 600204
120290	OSMED syndrome, 215150
120290	Stickler syndrome, type II, 184840
120435	Muir-Torre syndrome, 158320
120435	Colorectal cancer, hereditary, nonpolyposis, type 1 Ovarian cancer

120436	Muir-Torre family cancer syndrome, 158320
120436	Turcot syndrome with glioblastoma, 276300
120436	Colorectal cancer, hereditary nonpolyposis, type 2
120550	C1q deficiency, type A
120570	C1q deficiency, type B
120575	C1q deficiency, type C
120580	C1r/C1s deficiency, combined
120620	SLE susceptibility
120620	CR1 deficiency
120700	C3 deficiency
120810	C4 deficiency
120820	C4 deficiency
120920	Measles, susceptibility to
120950	C8 deficiency, type I
120960	C8 deficiency, type II
121014	Heterotaxia, viscerotaxial, autosomal recessive
121050	Contractural arachnodactyly, congenital
121800	Corneal dystrophy, crystalline, Schnyder
122720	Nicotine addiction, protection from
122720	Coumarin resistance, 122700
123270	[Creatine kinase, brain type, ectopic expression of]
123580	Cataract, congenital, autosomal dominant
123620	Cataract, cerulean, type 2, 601547
123660	Cataract, Coppock-like
123829	Melanoma
123940	White sponge nevus, 193900
124030	Parkinsonism, susceptibility to
124030	Debrisoquine sensitivity
124080	CMO II deficiency
124200	Darier disease (keratosis follicularis)
125264	Leukemia, acute nonlymphocytic
125270	Porphyria, acute hepatic
125270	Lead poisoning, susceptibility to
125490	Dentinogenesis imperfecta-1
125852	Insulin-dependent diabetes mellitus-2
126060	Anemia, megaloblastic, due to DHFR deficiency
126090	Hyperphenylalaninemia due to pterin-4a-carbinolamine dehydratase deficiency, 264070
126150	Diphtheria, susceptibility to
126340	Xeroderma pigmentosum, group D, 278730
126391	DNA ligase I deficiency
126451	Schizophrenia, susceptibility to
126452	Autonomic nervous system dysfunction
126452	[Novelty seeking personality]



126600	Doyne honeycomb retinal dystrophy
126600	Drusen, radial, autosomal dominant
126650	Chloride diarrhea, congenital, Finnish type, 214700
126650	Colon cancer
128100	Dystonia-1, torsion
129010	Neuropathy, congenital hypomyelinating, 1
129900	EEC syndrome-1
130410	Glutaricaciduria, type IIB
130500	Elliptocytosis-1
131100	Multiple endocrine neoplasia I
131100	Prolactinoma, hyperparathyroidism, carcinoid syndrome
131100	Carcinoid tumor of lung
131210	Atherosclerosis, susceptibility to
131242	Shah-Waardenburg syndrome, 277580
131400	Eosinophilia, familial
131440	Eosinophilic myeloproliferative disorder
131950	Epidermolysis bullosa, Ogna type
132700	Cylindromatosis
132800	Basal cell carcinoma
132800	Epithelioma, self-healing, squamous 1, Ferguson-Smith type
133170	Erythremia
133171	[Erythrocytosis, familial], 133100
133200	Erythrokeratoderma variabilis
133510	Trichothiodystrophy
133510	Xeroderma pigmentosum, group B
133700	Chondrosarcoma, 215300
133700	Exostoses, multiple, type 1
133701	Exostoses, multiple, type 2
133780	Vitreoretinopathy, exudative, familial
134370	Factor H deficiency
134370	Hemolytic-uremic syndrome, 235400
134370	Memproliferative glomerulonephritis
134570	Factor XIII A deficiency
134580	Factor XIII B deficiency
134638	Systemic lupus erythematosus, susceptibility, 152700
134790	Hyperferritinemia-cataract syndrome, 600886
134820	Dysfibrinogenemia, alpha type, causing bleeding diathesis
134820	Dysfibrinogenemia, alpha type, causing recurrent thrombosis
134820	Amyloidosis, hereditary renal, 105200
134830	Dysfibrinogenemia, beta type
134850	Dysfibrinogenemia, gamma type
134850	Hypofibrinogenemia, gamma type
134934	Thanatophoric dysplasia, types I and II, 187600
134934	Achondroplasia, 100800

134934	Craniosynostosis, nonsyndromic
134934	Crouzon syndrome with acanthosis nigricans
134934	Hypochondroplasia, 146000
135300	Fibromatosis, gingival
135600	Ehlers-Danlos syndrome, type X
135700	Fibrosis of extraocular muscles, congenital, 1
135940	Ichthyosis vulgaris, 146700
136132	[Fish-odor syndrome], 602079
136350	Pfeiffer syndrome, 101600
136435	Ovarian dysgenesis, hypergonadotropic, with normal karyotype, 233300
136530	Male infertility, familial
136550	Macular dystrophy, North Carolina type
136836	Fucosyltransferase-6 deficiency
137350	Amyloidosis, Finnish type, 105120
137600	Iridogoniodysgenesis syndrome
138030	[Hyperproglucagonemia]
138033	Diabetes mellitus, type II
138040	Cortisol resistance
138079	Hyperinsulinism, familial, 602485
138079	MODY, type 2, 125851
138140	Glucose transport defect, blood-brain barrier
138190	Diabetes mellitus, noninsulin-dependent
138320	Hemolytic anemia due to glutathione peroxidase deficiency
138570	Non-insulin dependent diabetes mellitus, susceptibility to
138700	[Apolipoprotein H deficiency]
138971	Kostmann neutropenia, 202700
138981	Pulmonary alveolar proteinosis, 265120
139130	Hypertension, essential, susceptibility to, 145500
139191	Growth hormone deficient dwarfism
139250	Isolated growth hormone deficiency, Illig type with absent GH and Kowarski type with bioinactive GH
139320	Pituitary ACTH secreting adenoma
139320	Pseudohypoparathyroidism, type Ia, 103580
139320	Somatotrophinoma
139320	McCune-Albright polyostotic fibrous dysplasia, 174800
139330	Night blindness, congenital stationary
139350	Epidermolytic hyperkeratosis, 113800
139350	Keratoderma, palmoplantar, nonepidermolytic
139360	Pituitary ACTH-secreting adenoma
141750	Alpha-thalassemia/mental retardation syndrome, type 1
141800	Methemoglobinemias, alpha-
141800	Thalassemias, alpha-
141800	Erythremias, alpha-

141800	Heinz body anemias, alpha-
141850	Thalassemia, alpha-
141850	Erythrocytosis
141850	Heinz body anemia
141850	Hemoglobin H disease
141850	Hypochromic microcytic anemia
141900	Methemoglobinemias, beta-
141900	Sickle cell anemia
141900	Thalassemias, beta-
141900	Erythremias, beta-
141900	HPFH, deletion type
141900	Heinz body anemias, beta-
142000	Thalassemia due to Hb Lepore
142000	Thalassemia, delta-
142200	HPFH, nondeletion type A
142250	HPFH, nondeletion type G
142270	Hereditary persistence of fetal hemoglobin
142335	Hereditary persistence of fetal hemoglobin, heterocellular, Indian type
142410	Non-insulin-dependent diabetes mellitus-2, 601407
142410	Insulin-dependent diabetes mellitus
142410	MODY, type 3, 600496
142470	[Hereditary persistence of fetal hemoglobin, heterocellular]
142600	Hemolytic anemia due to hexokinase deficiency
142640	Thrombophilia due to elevated HRG
142680	Periodic fever, familial
142857	Pemphigoid, susceptibility to
142858	Beryllium disease, chronic, susceptibility to
142946	Holoprosencephaly-4
142959	Hand-foot-uterus syndrome, 140000
142989	Synpolydactyly, type II, 186000
143100	Huntington disease
143200	Wagner syndrome
143200	Erosive vitreoretinopathy
143890	Hypercholesterolemia, familial
144120	Hyperimmunoglobulin G1 syndrome
144200	Epidermolytic palmoplantar keratoderma
145001	Hyperparathyroidism-jaw tumor syndrome
145260	Pseudohypoaldosteronism, type II
145981	Hypocalciuric hypercalcemia, type II
146150	Hypomelanosis of Ito
146150	Hypomelanosis of Ito
146200	Hypoparathyroidism, familial
146740	Neutropenia, alloimmune neonatal

146740	Viral infections, recurrent
146740	Lupus erythematosus, systemic, susceptibility, 152700
146790	Lupus nephritis, susceptibility to
147020	Agammaglobulinemia, 601495
147050	Atopy
147061	Allergy and asthma susceptibility
147110	IgG2 deficiency, selective
147141	Leukemia, acute lymphoblastic
147200	[Kappa light chain deficiency]
147280	Hepatocellular carcinoma
147440	Growth retardation with deafness and mental retardation
147450	Amyotrophic lateral sclerosis, due to SOD1 deficiency, 105400
147545	Diabetes mellitus, noninsulin-dependent
147570	Interferon, immune, deficiency
147575	Myelodysplastic syndrome, preleukemic
147575	Myelogenous leukemia, acute
147575	Macrocytic anemia refractory, of 5q- syndrome, 153550
147670	Rabson-Mendenhall syndrome
147670	Diabetes mellitus, insulin-resistant, with acanthosis nigricans
147670	Leprechaunism
147680	Severe combined immunodeficiency due to IL2 deficiency
147781	Atopy, susceptibility to
147790	Leukemia, acute lymphocytic, with 4/11 translocation
147791	Jacobsen syndrome
148040	Epidermolysis bullosa simplex, Koebner, Dowling-Meara, and Weber-Cockayne types, 131900, 131760, 131800
148041	Pachyonychia congenita, Jadassohn-Lewandowsky type, 167200
148043	Meesmann corneal dystrophy, 122100
148065	White sponge nevus, 193900
148066	Epidermolysis bullosa simplex, Koebner, Dowling-Meara, and Weber-Cockayne types, 131900, 131760, 131800
148066	Epidermolysis bullosa simplex, recessive, 601001
148067	Nonepidermolytic palmoplantar keratoderma, 600962
148067	Pachyonychia congenita, Jadassohn-Lewandowsky type, 167200
148069	Pachyonychia congenita, Jackson-Lawler type, 167210
148070	Liver disease, susceptibility to, from hepatotoxins or viruses
148080	Epidermolytic hyperkeratosis, 113800
148370	Keratolytic winter erythema
148500	Tylosis with esophageal cancer
150100	Lactate dehydrogenase-B deficiency
150200	[Placental lactogen deficiency]
150210	Lactoferrin-deficient neutrophils, 245480
150230	Langer-Giedion syndrome
150240	Cutis laxa, marfanoid neonatal type

150250	Larsen syndrome, autosomal dominant
150270	Laryngeal adductor paralysis
150292	Epidermolysis bullosa, Herlitz junctional type, 226700
150310	Epidermolysis bullosa, Herlitz junctional type, 226700
150310	Epidermolysis bullosa, generalized atrophic benign, 226650
151385	Leukemia, acute myeloid
151390	Leukemia, acute T-cell
151440	Leukemia, T-cell acute lymphoblastoid
151670	Hepatic lipase deficiency
152427	Long QT syndrome-2
152445	Vohwinkel syndrome, 124500
152445	Erythrokeratoderma, progressive symmetric, 602036
152760	Hypogonadotropic hypogonadism due to GNRH deficiency, 227200
152790	Precocious puberty, male, 176410
152790	Leydig cell hypoplasia
153455	Cutis laxa, recessive, type I, 219100
153700	Macular dystrophy, vitelliform type
153840	Macular dystrophy, atypical vitelliform
153880	Macular dystrophy, dominant cystoid
154275	Malignant hyperthermia susceptibility 2
154276	Malignant hyperthermia susceptibility 3
154550	Carbohydrate-deficient glycoprotein syndrome, type Ib, 602579
154705	Marfan syndrome, type II
155600	Malignant melanoma, cutaneous
156225	Muscular dystrophy, congenital merosin-deficient
156232	Mesomelic dysplasia, Kantaputra type
156490	Neuroblastoma
156850	Cataract, congenital, with microphthalmia
157170	Holoprosencephaly-2
157640	PEO with mitochondrial DNA deletions, type 1
157655	Lactic acidosis due to defect in iron-sulfur cluster of complex I
157900	Moebius syndrome
158590	Spinal muscular atrophy-4
158900	Facioscapulohumeral muscular dystrophy-1A
159000	Muscular dystrophy, limb-girdle, type 1A
159001	Muscular dystrophy, limb-girdle, type 1B
159440	Charcot-Marie-Tooth neuropathy-1B, 118200
159440	Dejerine-Sottas disease, myelin P-related, 145900
159440	Hypomyelination, congenital
159555	Leukemia, myeloid/lymphoid or mixed-lineage
159595	Leukemia, transient, of Down syndrome
160760	Cardiomyopathy, familial hypertrophic, 1, 192600
160760	Central core disease, one form

160781	Cardiomyopathy, hypertrophic, mid-left ventricular chamber type
160900	Myotonic dystrophy
160980	Carney myxoma-endocrine complex
161015	Mitochondrial complex I deficiency, 252010
162100	Neuralgic amyotrophy with predilection for brachial plexus
162200	Neurofibromatosis, type 1
162200	Watson syndrome, 193520
163729	Hypertension; pregnancy-induced
163950	Noonan syndrome-1
163950	Cardiofaciocutaneous syndrome, 115150
164009	Leukemia, acute promyelocytic, NUMA/RARA type
164160	Obesity, severe, due to leptin deficiency
164200	Oculodentodigital dysplasia
164200	Syndactyly, type III, 186100
164500	Spinocerebellar ataxia-7
164731	Ovarian carcinoma, 167000
164860	Renal cell carcinoma, papillary, familial and sporadic
164953	Liposarcoma
165320	Hepatocellular carcinoma
165500	Optic atrophy 1
167000	Ovarian cancer, serous
167250	Paget disease of bone
168000	Paraganglioma, familial nonchromaffin, 1
168360	Paraneoplastic sensory neuropathy
168461	Multiple myeloma, 254250
168461	Parathyroid adenomatosis 1
168461	Centrocytic lymphoma
168468	Metaphyseal chondrodysplasia, Murk Jansen type, 156400
168470	Humoral hypercalcemia of malignancy
168500	Parietal foramina
168610	Parkinsonism-dementia with pallidopontonigral degeneration
169600	Hailey-Hailey disease
170261	Bare lymphocyte syndrome, type I, due to TAP2 deficiency
170500	Myotonia congenita, atypical acetazolamide-responsive
170500	Paramyotonia congenita, 168300
170500	Hyperkalemic periodic paralysis
170995	Zellweger syndrome-2
171050	Colchicine resistance
171060	Cholestasis, progressive familial intrahepatic, type III, 602347
171190	Hypertension, essential, 145500
171650	Lysosomal acid phosphatase deficiency
171760	Hypophosphatasia, adult, 146300
171760	Hypophosphatasia, infantile, 241500
171860	Hemolytic anemia due to phosphofructokinase deficiency

172400	Hemolytic anemia due to glucosephosphate isomerase deficiency
172400	Hydrops fetalis, one form
172411	Colorectal cancer, resistance to
172471	Glycogenosis, hepatic, autosomal
172490	Phosphorylase kinase deficiency of liver and muscle, 261750
173350	Plasminogen Tochigi disease
173350	Plasminogen deficiency, types I and II
173350	Thrombophilia, dysplasminogenemic
173360	Thrombophilia due to excessive plasminogen activator inhibitor
173360	Hemorrhagic diathesis due to PAI1 deficiency
173610	Platelet alpha/delta storage pool deficiency
173850	Polio, susceptibility to
173870	Xeroderma pigmentosum
173870	Fanconi anemia
173910	Polycystic kidney disease, adult, type II
174000	Medullary cystic kidney disease, AD
174900	Polyposis, juvenile intestinal
175100	Turcot syndrome, 276300
175100	Adenomatous polyposis coli
175100	Adenomatous polyposis coli, attenuated
175100	Colorectal cancer
175100	Desmoid disease, hereditary, 135290
175100	Gardner syndrome
176100	Porphyria cutanea tarda
176100	Porphyria, hepatoerythropoietic
176260	Episodic ataxia/myokymia syndrome, 160120
176261	Jervell and Lange-Nielsen syndrome, 220400
176300	[Dystransthyretinemic hyperthyroxinemia]
176300	Carpal tunnel syndrome, familial
176300	Amyloid neuropathy, familial, several allelic types
176300	Amyloidosis, senile systemic
176310	Leukemia, acute pre-B-cell
176450	Sacral agenesis-1
176640	Creutzfeldt-Jakob disease, 123400
176640	Gerstmann-Straussler disease, 137440
176640	Insomnia, fatal familial
176705	Breast cancer, sporadic
176730	Diabetes mellitus, rare form
176730	Hyperproinsulinemia, familial
176730	MODY, one form
176930	Dysprothrombinemia
176930	Hypoprothrombinemia
176960	Pituitary tumor, invasive
177070	Spherocytosis, hereditary, Japanese type

177070	Hermansky-Pudlak syndrome, 203300
177900	Psoriasis susceptibility-1
178300	Ptosis, hereditary congenital, 1
178600	Pulmonary hypertension, familial primary
178640	Pulmonary alveolar proteinosis, congenital, 265120
179095	Male infertility
179450	Ragweed sensitivity
179615	Reticulosis, familial histiocytic, 267700
179615	Severe combined immunodeficiency, B cell-negative, 601457
179616	Severe combined immunodeficiency, B cell-negative, 601457
179755	Renal cell carcinoma, papillary, 1
179820	[Hyperproreninemia]
180020	Retinal cone dystrophy-1
180069	Retinal dystrophy, autosomal recessive, childhood-onset
180069	Retinitis pigmentosa-20
180069	Leber congenital amaurosis-2, 204100
180071	Retinitis pigmentosa, autosomal recessive
180072	Night blindness, congenital stationary, type 3, 163500
180072	Retinitis pigmentosa, autosomal recessive
180100	Retinitis pigmentosa-1
180104	Retinitis pigmentosa-9
180105	Retinitis pigmentosa-10
180240	Leukemia, acute promyelocytic
180250	Retinol binding protein, deficiency of
180297	Anemia, hemolytic, Rh-null, suppressor type, 268150
180380	Night blindness, congenital stationery, rhodopsin-related
180380	Retinitis pigmentosa, autosomal recessive
180380	Retinitis pigmentosa-4, autosomal dominant
180385	Leukemia, acute T-cell
180721	Retinitis pigmentosa, digenic
180840	Susceptibility to IDDM
180860	Russell-Silver syndrome
180901	Malignant hyperthermia susceptibility 1, 145600
180901	Central core disease, 117000
181405	Scapuloperoneal spinal muscular atrophy, New England type
181430	Scapuloperoneal syndrome, myopathic type
181460	Schistosoma mansoni, susceptibility/resistance to
181510	Schizophrenia
181600	Sclerolylosis
182138	Anxiety-related personality traits
182280	Small-cell cancer of lung
182380	Glucose/galactose malabsorption
182381	Renal glucosuria, 253100
182452	Lung cancer, small cell



182500	Cataract, congenital
182600	Spastic paraplegia-3A
182601	Spastic paraplegia-4
182860	Pyropoikilocytosis
182860	Spherocytosis, recessive
182860	Elliptocytosis-2
182870	Spherocytosis-1
182870	Elliptocytosis-3
182870	Anemia, neonatal hemolytic, fatal and near-fatal
182900	Spherocytosis-2
185470	Myopathy due to succinate dehydrogenase deficiency
185800	Symphalangism, proximal
186580	Arthrocutaneouveal granulomatosis
186740	Immunodeficiency due to defect in CD3-gamma
186770	Leukemia, T-cell acute lymphocytic
186780	CD3, zeta chain, deficiency
186830	Immunodeficiency, T-cell receptor/CD3 complex
186855	Leukemia-2, T-cell acute lymphoblastic
186860	Leukemia/lymphoma, T-cell
186880	Leukemia/lymphoma, T-cell
186921	Leukemia, T-cell acute lymphoblastic
187040	Leukemia-1, T-cell acute lymphoblastic
188025	Thrombocytopenia, Paris-Trousseau type
188070	Bleeding disorder due to defective thromboxane A2 receptor
188540	Hypothyroidism, nongoitrous
188826	Sorsby fundus dystrophy, 136900
189800	Preeclampsia/eclampsia
190000	Atransferrinemia
190020	Bladder cancer, 109800
190040	Dermatofibrosarcoma protuberans
190040	Giant-cell fibroblastoma
190040	Meningioma, SIS-related
190070	Colorectal adenoma
190070	Colorectal cancer
190080	Burkitt lymphoma
190100	Geniospasm
190195	Ichthyosiform erythroderma, congenital, 242100
190195	Ichthyosis, lamellar, autosomal recessive, 242300
190300	Tremor, familial essential, 1
190350	Trichorhinophalangeal syndrome, type I
190450	Hemolytic anemia due to triosephosphate isomerase deficiency
190605	Triphalangeal thumb-polysyndactyly syndrome
190685	Down syndrome
190900	Colorblindness, tritan

191010	Cardiomyopathy, familial hypertrophic, 3, 115196
191030	Nemaline myopathy-1, 161800
191044	Cardiomyopathy, familial hypertrophic
191045	Cardiomyopathy, familial hypertrophic, 2, 115195
191092	Tuberous sclerosis-2
191100	Tuberous sclerosis-1
191181	Cervical carcinoma
191290	Segawa syndrome, recessive
191315	Insensitivity to pain, congenital, with anhidrosis, 256800
192340	Diabetes insipidus, neurohypophyseal, 125700
192500	Jervell and Lange-Nielsen syndrome, 220400
192500	Long QT syndrome-1
192974	Neonatal alloimmune thrombocytopenia
192974	Glycoprotein Ia deficiency
193235	Vitreoretinopathy, neovascular inflammatory
193300	Renal cell carcinoma
193300	von Hippel-Lindau syndrome
194070	Wilms tumor, type 1
194070	Denys-Drash syndrome
194070	Frasier syndrome, 136680
194071	Wilms tumor, type 2
194071	Adrenocortical carcinoma, hereditary, 202300
194190	Wolf-Hirschhorn syndrome
200150	Choreoacanthocytosis
200350	Acetyl-CoA carboxylase deficiency
200990	Acrocallosal syndrome
201450	Acyl-CoA dehydrogenase, medium chain, deficiency of
201460	Acyl-CoA dehydrogenase, long chain, deficiency of
201470	Acyl-CoA dehydrogenase, short-chain, deficiency of
201810	3-beta-hydroxysteroid dehydrogenase, type II, deficiency
201910	Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency
202010	Adrenal hyperplasia, congenital, due to 11-beta-hydroxylase deficiency
202010	Aldosteronism, glucocorticoid-remediable
202200	Glucocorticoid deficiency, due to ACTH unresponsiveness
203100	Waardenburg syndrome/ocular albinism, digenic, 103470
203100	Albinism, oculocutaneous, type IA
203310	Ocular albinism, autosomal recessive
203500	Alkaptonuria
203750	3-ketothiolase deficiency
203800	Alstrom syndrome
204500	Ceroid-lipofuscinosis, neuronal 2, classic late infantile
205100	Amyotrophic lateral sclerosis, juvenile
205900	Anemia, Diamond-Blackfan

207750	Hyperlipoproteinemia, type Ib
207800	Argininemia
208250	Jacobs syndrome
209900	Bardet-Biedl syndrome 2
209901	Bardet-Biedl syndrome 1
211420	Breast cancer, ductal
213700	Cerebrotendinous xanthomatosis
214400	Charcot-Marie-Tooth neuropathy-4A
215700	Citrullinemia
216900	Achromatopsia
216950	C1r/C1s deficiency, combined
217000	C2 deficiency
217030	C3b inactivator deficiency
217300	Cornea plana congenita, recessive
218000	Andermann syndrome
221770	Polycystic lipomembranous osteodysplasia with sclerosing leukencephalopathy
221820	Gliososis, familial progressive subcortical
222100	Diabetes mellitus, insulin-dependent-1
222700	Lysinuric protein intolerance
222800	Hemolytic anemia due to bisphosphoglycerate mutase deficiency
222900	Sucrose intolerance
223000	Lactase deficiency, adult, 223100
223000	Lactase deficiency, congenital
223360	Dopamine-beta-hydroxylase deficiency
223900	Dysautonomia, familial
227220	[Eye color, brown]
227400	Thromboembolism susceptibility due to factor V Leiden
227400	Hemorrhagic diathesis due to factor V deficiency
227646	Fanconi anemia, type D
228960	[Kininogen deficiency]
229000	Fletcher factor deficiency
229300	Friedreich ataxia
229300	Friedreich ataxia with retained reflexes
229600	Fructose intolerance
230000	Fucosidosis
230200	Galactokinase deficiency with cataracts
230350	Galactose epimerase deficiency
230400	Galactosemia
230450	Hemolytic anemia due to gamma-glutamylcysteine synthetase deficiency
230800	Gaucher disease
230800	Gaucher disease with cardiovascular calcification
231550	Achalasia-addisonianism-alacrimia syndrome

231670	Glutaricaciduria, type I
231680	Glutaricaciduria, type IIA
231950	Glutathioninuria
232050	Propionicacidemia, type II or pccB type
232200	Glycogen storage disease I
232600	McArdle disease
232700	Glycogen storage disease VI
233100	[Renal glucosuria]
233700	Chronic granulomatous disease due to deficiency of NCF-1
233710	Chronic granulomatous disease due to deficiency of NCF-2
234200	Neurodegeneration with brain iron accumulation
235200	Hemochromatosis
235800	[Histidinemia]
236100	Holoprosencephaly-1
236200	Homocystinuria, B6-responsive and nonresponsive types
236700	McKusick-Kaufman syndrome
236730	Urofacial syndrome
238600	Chylomicronemia syndrome, familial
238600	Combined hyperlipemia, familial
238600	Hyperlipoproteinemia I
238600	Lipoprotein lipase deficiency
239100	Van Buchem disease
240300	Autoimmune polyglandular disease, type I
243500	Isovalericacidemia
245200	Krabbe disease
245349	Lacticacidemia due to PDX1 deficiency
246450	HMG-CoA lyase deficiency
246900	Lipoamide dehydrogenase deficiency
247200	Miller-Dieker lissencephaly syndrome
248510	Mannosidosis, beta-
248600	Maple syrup urine disease, type Ia
248610	Maple syrup urine disease, type II
248611	Maple syrup urine disease, type Ib
249000	Meckel syndrome
250100	Metachromatic leukodystrophy
250250	Cartilage-hair hypoplasia
250800	Methemoglobinemia, type I
250800	Methemoglobinemia, type II
250850	Hypermethioninemia, persistent, autosomal dominant, due to methionine adenosyltransferase I/III deficiency
251000	Methylmalonicaciduria, mutase deficiency type
251170	Mevalonicaciduria
251600	Microphthalmia, autosomal recessive
252500	Mucopolipidosis II

252500	Mucopolipidosis III
252800	Mucopolysaccharidosis Ih
252800	Mucopolysaccharidosis Ih/s
252800	Mucopolysaccharidosis Is
252920	Sanfilippo syndrome, type B
252940	Sanfilippo syndrome, type D
253200	Maroteaux-Lamy syndrome, several forms
253250	Mulibrey nanism
253260	Biotinidase deficiency
253270	Multiple carboxylase deficiency, biotin-responsive
253800	Walker-Warburg syndrome, 236670
253800	Fukuyama type congenital muscular dystrophy
254210	Myasthenia gravis, familial infantile
255800	Schwartz-Jampel syndrome
256030	Nemaline myopathy-2
256540	Galactosialidosis
256550	Sialidosis, type I
256550	Sialidosis, type II
258501	3-methylglutaconicaciduria, type III
258900	Oroticaciduria
259700	Osteopetrosis, recessive
259770	Osteoporosis-pseudoglioma syndrome
259900	Hyperoxaluria, primary, type 1
261510	Pseudo-Zellweger syndrome
261515	Peroxisomal bifunctional enzyme deficiency
261600	Phenylketonuria
261600	[Hyperphenylalaninemia, mild]
261640	Phenylketonuria due to PTS deficiency
262000	Bjornstad syndrome
263200	Polycystic kidney disease, autosomal recessive
263700	Porphyria, congenital erythropoietic
264300	Pseudohermaphroditism, male, with gynecomastia
264470	Adrenoleukodystrophy, pseudoneonatal
264700	Pseudo-vitamin D dependency rickets 1
264900	Factor XI deficiency
266100	Pyridoxine dependency with seizures
266150	Pyruvate carboxylase deficiency
266200	Anemia, hemolytic, due to PK deficiency
266300	[Hair color, red]
267750	Knobloch syndrome
268800	Sandhoff disease, infantile, juvenile, and adult forms
268800	Spinal muscular atrophy, HEXB-related
268900	[Sarcosinemia]
269920	Salla disease

270100	Situs inversus viscerum
271245	Spinocerebellar ataxia-8, infantile, with sensory neuropathy
271900	Canavan disease
272800	Tay-Sachs disease
272800	[Hex A pseudodeficiency]
272800	GM2-gangliosidosis, juvenile, adult
273300	Male germ cell tumor
274600	Pendred syndrome
274600	Deafness, autosomal recessive 4
276000	Pancreatitis, hereditary, 167800
276000	Trypsinogen deficiency
276700	Tyrosinemia, type I
276710	Tyrosinemia, type III
276900	Usher syndrome, type 1A
276901	Usher syndrome, type 2
276902	Usher syndrome, type 3
276903	Usher syndrome, type 1B
276903	Deafness, autosomal dominant 11, neurosensory, 601317
276903	Deafness, autosomal recessive 2, neurosensory, 600060
277700	Werner syndrome
277730	Wernicke-Korsakoff syndrome, susceptibility to
277900	Wilson disease
278000	Wolman disease
278000	Cholesteryl ester storage disease
278300	Xanthinuria, type I
278700	Xeroderma pigmentosum, group A
278720	Xeroderma pigmentosum, group C
300008	Nephrolithiasis, type I, 310468
300008	Proteinuria, low molecular weight, with hypercalciuric nephrocalcinosis
300008	Dent disease, 300009
300008	Hypophosphatemia, type III
300031	Mental retardation, X-linked, FRAXF type
300044	Wernicke-Korsakoff syndrome, susceptibility to
300047	Mental retardation, X-linked 20
300048	Intestinal pseudoobstruction, neuronal, X-linked
300049	Nodular heterotopia, bilateral periventricular
300049	BPNH/MR syndrome
300055	Mental retardation with psychosis, pyramidal signs, and macroorchidism
300071	Night blindness, congenital stationary, type 2
300100	Adrenoleukodystrophy
300100	Adrenomyeloneuropathy
300104	Mental retardation, X-linked nonspecific, 309541

300110	Night blindness, congenital stationary, X-linked incomplete, 300071
300126	Dyskeratosis congenita-1, 305000
300600	Ocular albinism, Forsius-Eriksson type
301000	Thrombocytopenia, X-linked, 313900
301000	Wiskott-Aldrich syndrome
301201	Amelogenesis imperfecta-3, hypoplastic type
301590	Anophthalmos-1
301830	Arthrogryposis, X-linked (spinal muscular atrophy, infantile, X-linked)
301835	Arts syndrome
302060	Noncompaction of left ventricular myocardium, isolated
302060	Barth syndrome
302060	Cardiomyopathy, X-linked dilated, 300069
302060	Endocardial fibroelastosis-2
302960	Chondrodysplasia punctata, X-linked dominant
303700	Colorblindness, blue monochromatic
303800	Colorblindness, deutan
303900	Colorblindness, protan
304040	Charcot-Marie-Tooth neuropathy, X-linked-1, dominant, 302800
304800	Diabetes insipidus, nephrogenic
305100	Anhidrotic ectodermal dysplasia
305450	FG syndrome
305900	Favism
305900	G6PD deficiency
305900	Hemolytic anemia due to G6PD deficiency
306700	Hemophilia A
306995	[Homosexuality, male]
308310	Incontinentia pigmenti, familial
308840	Spastic paraplegia, 312900
308840	Hydrocephalus due to aqueductal stenosis, 307000
308840	MASA syndrome, 303350
309200	Manic-depressive illness, X-linked
309470	Mental retardation, X-linked, syndromic-3, with spastic diplegia
309500	Renpenning syndrome-1
309548	Mental retardation, X-linked, FRAXE type
309605	Mental retardation, X-linked, syndromic-4, with congenital contractures and low fingertip arches
309610	Mental retardation, X-linked, syndromic-2, with dysmorphism and cerebral atrophy
309620	Mental retardation-skeletal dysplasia
309850	Brunner syndrome
309900	Mucopolysaccharidosis II
310300	Emery-Dreifuss muscular dystrophy

310400	Myotubular myopathy, X-linked
310460	Myopia-1
310460	Bornholm eye disease
311050	Optic atrophy, X-linked
311300	Otopalatodigital syndrome, type I
311510	Waisman parkinsonism-mental retardation syndrome
311850	Phosphoribosyl pyrophosphate synthetase-related gout
312060	Properdin deficiency, X-linked
312760	Turner syndrome
313700	Perineal hypospadias
313700	Prostate cancer
313700	Spinal and bulbar muscular atrophy of Kennedy, 313200
313700	Breast cancer, male, with Reifenstein syndrome
313700	Androgen insensitivity, several forms
314250	Dystonia-3, torsion, with parkinsonism, Filipino type
314300	Goeminne TKCR syndrome
314400	Cardiac valvular dysplasia-1
314580	Wieacker-Wolff syndrome
600040	Colorectal cancer
600044	Thrombocythemia, essential, 187950
600045	Xeroderma pigmentosum, group E, subtype 2
600048	Breast cancer-3
600059	Retinitis pigmentosa-13
600065	Leukocyte adhesion deficiency, 116920
600079	Colon cancer
600095	Split hand/foot malformation, type 3
600101	Deafness, autosomal dominant 2
600105	Retinitis pigmentosa-12, autosomal recessive
600119	Muscular dystrophy, Duchenne-like, type 2
600119	Adhalinopathy, primary
600138	Retinitis pigmentosa-11
600140	Rubenstein-Taybi syndrome, 180849
600143	Epilepsy, progressive, with mental retardation
600163	Long QT syndrome-3
600173	SCID, autosomal recessive, T-negative/B-positive type
600175	Spinal muscular atrophy, congenital nonprogressive, of lower limbs
600179	Leber congenital amaurosis, type I, 204000
600185	Pancreatic cancer
600185	Breast cancer 2, early onset
600194	Ichthyosis bullosa of Siemens, 146800
600202	Dyslexia, specific, 2
600211	Cleidocranial dysplasia, 119600
600228	Pseudohypoadosteronism, type I, 264350



600231	Palmoplantar keratoderma, Bothnia type
600234	HMG-CoA synthase-2 deficiency
600243	Temperature-sensitive apoptosis
600258	Colorectal cancer, hereditary nonpolyposis, type 3
600259	Turcot syndrome with glioblastoma, 276300
600259	Colorectal cancer, hereditary nonpolyposis, type 4
600261	Ehlers-Danlos-like syndrome
600273	Polycystic kidney disease, infantile severe, with tuberous sclerosis
600276	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, 125310
600281	Non-insulin-dependent diabetes mellitus, 125853
600281	MODY, type 1, 125850
600309	Atrioventricular canal defect-1
600310	Pseudoachondroplasia, 177170
600310	Epiphyseal dysplasia, multiple 1, 132400
600319	Diabetes mellitus, insulin-dependent, 4
600320	Insulin-dependent diabetes mellitus-5
600321	Diabetes mellitus, insulin-dependent, 7
600332	Rippling muscle disease-1
600354	Spinal muscular atrophy-1, 253300
600354	Spinal muscular atrophy-2, 253550
600354	Spinal muscular atrophy-3, 253400
600374	Bardet-Biedl syndrome 4
600414	Adrenoleukodystrophy, neonatal, 202370
600415	Ataxia with isolated vitamin E deficiency, 277460
600429	[Ii blood group, 110800]
600430	Brachydactyly-mental retardation syndrome
600467	Malignant hyperthermia susceptibility 4
600510	Pigment dispersion syndrome
600511	Schizophrenia-3
600512	Epilepsy, partial
600525	Trichodontoosseous syndrome, 190320
600528	CPT deficiency, hepatic, type I, 255120
600536	Myopathy, congenital
600542	Chondrosarcoma, extraskeletal myxoid
600617	Lipoid adrenal hyperplasia, 201710
600618	Leukemia, acute lymphoblastic
600623	Prostate cancer, 176807
600631	Enuresis, nocturnal, 1
600650	Myopathy due to CPT II deficiency, 255110
600650	CPT deficiency, hepatic, type II, 600649
600652	Deafness, autosomal dominant 4
600669	Epilepsy, generalized, idiopathic
600678	Cancer susceptibility

600700	Lipoma
600701	Lipoma
600722	Ceroid lipofuscinosis, neuronal, variant juvenile type, with granular osmiophilic deposits
600722	Ceroid lipofuscinosis, neuronal-1, infantile, 256730
600725	Holoprosencephaly-3, 142945
600757	Orofacial cleft-3
600759	Alzheimer disease-4
600792	Deafness, autosomal recessive 5
600807	Bronchial asthma
600808	Enuresis, nocturnal, 2
600811	Xeroderma pigmentosum, group E, DDB-negative subtype, 278740
600839	Bartter syndrome, 241200
600850	Schizophrenia disorder-4
600856	Beckwith-Wiedemann syndrome, 130650
600881	Cataract, congenital, zonular, with sutural opacities
600882	Charcot-Marie-Tooth neuropathy-2B
600883	Diabetes mellitus, insulin-dependent, 8
600884	Cardiomyopathy, familial dilated 1B
600887	Endometrial carcinoma
600897	Cataract, zonular pulverulent-1, 116200
600899	Severe combined immunodeficiency, type I, 202500
600918	Cystinuria, type III
600919	Long QT syndrome-4 with sinus bradycardia
600923	Porphyria variegata, 176200
600956	Persistent Mullerian duct syndrome, type II, 261550
600957	Persistent Mullerian duct syndrome, type I, 261550
600958	Cardiomyopathy, familial hypertrophic, 4, 115197
600964	Refsum disease, adult, with increased pipecolicacidemia
600965	Deafness, autosomal dominant 6
600968	Gitelman syndrome, 263800
600971	Deafness, autosomal recessive 6
600974	Deafness, autosomal recessive 7
600975	Glaucoma 3, primary infantile, B
600977	Cone dystrophy, progressive
600994	Deafness, autosomal dominant 5
600995	Nephrotic syndrome, idiopathic, steroid-resistant
600996	Arrhythmogenic right ventricular dysplasia-2
600998	Bleeding diathesis due to GNAQ deficiency
601011	Spinocerebellar ataxia-6, 183086
601011	Cerebellar ataxia, pure
601011	Episodic ataxia, type 2, 108500
601011	Hemiplegic migraine, familial, 141500

601071	Deafness, autosomal recessive 9
601072	Deafness, autosomal recessive 8
601105	Pycnodysostosis, 265800
601107	Dubin-Johnson syndrome, 237500
601130	Tolbutamide poor metabolizer
601145	Epilepsy, progressive myoclonic 1, 254800
601154	Cardiomyopathy, dilated, 1E
601199	Neonatal hyperparathyroidism, 239200
601199	Hypocalcemia, autosomal dominant, 601198
601199	Hypocalciuric hypercalcemia, type I, 145980
601202	Cataract, anterior polar-2
601208	Insulin-dependent diabetes mellitus-11
601226	Progressive external ophthalmoplegia, type 2
601238	Cerebellar ataxia, Cayman type
601253	Muscular dystrophy, limb-girdle, type IC
601267	HIV infection, susceptibility/resistance to
601277	Ichthyosis, lamellar, type 2
601282	Muscular dystrophy with epidermolysis bullosa simplex, 226670
601284	Hereditary hemorrhagic telangiectasia-2, 600376
601313	Polycystic kidney disease, adult type I, 173900
601316	Deafness, autosomal dominant 10
601318	Diabetes mellitus, insulin-dependent, 13
601363	Wilms tumor, type 4
601369	Deafness, autosomal dominant 9
601373	HIV infection, susceptibility/resistance to
601382	Charcot-Marie-Tooth neuropathy-4B
601385	Prostate cancer
601386	Deafness, autosomal recessive 12
601399	Platelet disorder, familial, with associated myeloid malignancy
601406	B-cell non-Hodgkin lymphoma, high-grade
601410	Diabetes mellitus, transient neonatal
601412	Deafness, autosomal dominant 7
601414	Retinitis pigmentosa-18
601455	Hereditary motor and sensory neuropathy, Lom type
601471	Moebius syndrome-2
601493	Cardiomyopathy, dilated 1C
601494	Cardiomyopathy, familial, dilated-2
601499	Rieger syndrome, type 2
601517	Spinocerebellar ataxia-2, 183090
601518	Prostate cancer, hereditary, 1, 176807
601542	Rieger syndrome, type 1, 180500
601545	Lissencephaly-1
601556	Spinocerebellar ataxia-1, 164400
601596	Charcot-Marie-Tooth neuropathy, demyelinating

601604	Mycobacterial and salmonella infections, susceptibility to
601620	Holt-Oram syndrome, 142900
601621	Ulnar-mammary syndrome, 181450
601622	Saethre-Chotzen syndrome, 101400
601623	Angelman syndrome
601649	Blepharophimosis, epicanthus inversus, and ptosis, type 2
601650	Paraganglioma, familial nonchromaffin, 2
601652	Glaucoma 1A, primary open angle, juvenile-onset, 137750
601653	Branchiotoic syndrome
601653	Branchiotoicorenal syndrome, 113650
601666	Insulin-dependent diabetes mellitus-15
601669	Hirschsprung disease, one form
601676	Acute insulin response
601680	Distal arthrogryposis, type 2B
601682	Glaucoma 1C, primary open angle
601687	Meesmann corneal dystrophy, 122100
601690	Platelet-activating factor acetylhydrolase deficiency
601691	Retinitis pigmentosa-19, 601718
601691	Stargardt disease-1, 248200
601691	Cone-rod dystrophy 3
601691	Fundus flavimaculatus with macular dystrophy, 248200
601692	Reis-Bucklers corneal dystrophy
601692	Corneal dystrophy, Avellino type
601692	Corneal dystrophy, Groenouw type I, 121900
601692	Corneal dystrophy, lattice type I, 122200
601718	Retinitis pigmentosa-19
601744	Systemic lupus erythematosus, susceptibility to, 1
601757	Rhizomelic chondrodysplasia punctata, type 1, 215100
601768	Leukemia, acute myeloid
601769	Osteoporosis, involutional
601769	Rickets, vitamin D-resistant, 277440
601771	Glaucoma 3A, primary infantile, 231300
601777	Cone dystrophy, progressive
601780	Ceroid-lipofuscinosis, neuronal-6, variant late infantile
601785	Carbohydrate-deficient glycoprotein syndrome, type I, 212065
601800	[Hair color, brown]
601843	Hypothyroidism, congenital, 274400
601844	Pseudohypoaldosteronism type II
601846	Muscular dystrophy with rimmed vacuoles
601850	Retinitis pigmentosa-deafness syndrome
601863	Bare lymphocyte syndrome, complementation group C
601868	Deafness, autosomal dominant 13
601884	[High bone mass]
601889	Lymphoma, diffuse large cell

601920	Alagille syndrome, 118450
601928	Monilethrix, 158000
601954	Muscular dystrophy, limb-girdle, type 2G
601969	Glioblastoma multiforme, 137800
601969	Medulloblastoma, 155255
601975	Ectodermal dysplasia/skin fragility syndrome
601990	Neuroblastoma
602011	Pancreatic endocrine tumors
602014	Hypomagnesemia with secondary hypocalcemia
602023	Bartter syndrome, type 3
602025	Obesity/hyperinsulinism, susceptibility to
602026	Refsum disease, 266500
602067	Cardiomyopathy, dilated, 1F
602081	Speech-language disorder-1
602082	Corneal dystrophy, Thiel-Behnke type
602086	Arrhythmogenic right ventricular dysplasia-3
602087	Arrhythmogenic right ventricular dysplasia-4
602088	Nephronophthisis, infantile
602089	Hemangioma, capillary, hereditary
602091	Marfan syndrome, atypical
602092	Deafness, autosomal recessive 18
602094	Lipodystrophy, familial partial
602096	Alzheimer disease-5
602116	Glioma
602117	Prader-Willi syndrome
602121	Deafness, autosomal dominant nonsyndromic sensorineural, 1, 124900
602134	Tremor, familial essential, 2
602136	Refsum disease, infantile, 266510
602136	Zellweger syndrome-1, 214100
602136	Adrenoleukodystrophy, neonatal, 202370
602153	Monilethrix, 158000
602216	Peutz-Jeghers syndrome, 175200
602225	Cone-rod retinal dystrophy-2, 120970
602225	Leber congenital amaurosis, type III
602232	Epilepsy, benign neonatal, type 2, 121201
602235	Epilepsy, benign, neonatal, type 1, 121200
602279	Oculopharyngeal muscular dystrophy, 164300
602279	Oculopharyngeal muscular dystrophy, autosomal recessive, 257950
602280	Retinitis pigmentosa-14, 600132
602403	Alzheimer disease, susceptibility to
602404	Parkinson disease, type 3
602421	Sweat chloride elevation without CF

602421	Congenital bilateral absence of vas deferens, 277180
602421	Cystic fibrosis, 219700
602447	Coronary artery disease, susceptibility to
602460	Deafness, autosomal dominant 15, 602459
602475	Ossification of posterior longitudinal ligament of spine
602476	Febrile convulsions, familial, 1
602477	Febrile convulsions, familial, 2
602491	Hyperlipidemia, familial combined, 1
602522	Bartter syndrome, infantile, with sensorineural deafness
602544	Parkinson disease, juvenile, type 2, 600116
602574	Deafness, autosomal dominant 12, 601842
602574	Deafness, autosomal dominant 8, 601543
602616	Carbohydrate-deficient glycoprotein syndrome, type II, 212066
602629	Dystonia-6, torsion
602631	Rhabdomyosarcoma, 268210
602631	Breast Cancer
602667	Nijmegen breakage syndrome, 251260
602716	Nephrosis-1, congenital, Finnish type, 256300
602771	Muscular dystrophy, congenital, with early spine rigidity
602772	Retinitis pigmentosa-24
602782	Faisalabad histiocytosis

### *Polynucleotide and Polypeptide Variants*

[0071] The present invention is also directed to variants of the ovarian associated polynucleotide sequence disclosed in SEQ ID NO:X or the complementary strand thereto, nucleotide sequences encoding the polypeptide of SEQ ID NO:Y, the nucleotide sequence of SEQ ID NO:X encoding the polypeptide sequence as defined in column 6 of Table 1, nucleotide sequences encoding the polypeptide as defined in column 6 of Table 1, the nucleotide sequence as defined in columns 8 and 9 of Table 2, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, the cDNA sequence contained in Clone ID NO:Z, and/or nucleotide sequences encoding a polypeptide encoded by the cDNA sequence contained in Clone ID NO:Z.

[0072] The present invention also encompasses variants of the polypeptide sequence disclosed in SEQ ID NO:Y, a polypeptide sequence as defined in column 6 of

Table 1, a polypeptide sequence encoded by the polynucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, and/or a polypeptide sequence encoded by the cDNA sequence contained in Clone ID NO:Z.

[0073] "Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

[0074] Thus, one aspect of the invention provides an isolated nucleic acid molecule comprising, or alternatively consisting of, a polynucleotide having a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence described in SEQ ID NO:X or contained in the cDNA sequence of Clone ID NO:Z; (b) a nucleotide sequence in SEQ ID NO:X or the cDNA in Clone ID NO:Z which encodes a mature ovarian associated polypeptide; (c) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of Clone ID NO:Z, which encodes a biologically active fragment of an ovarian associated polypeptide; (d) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of Clone ID NO:Z, which encodes an antigenic fragment of an ovarian associated polypeptide; (e) a nucleotide sequence encoding an ovarian associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (f) a nucleotide sequence encoding a mature ovarian associated polypeptide of the amino acid sequence of SEQ ID NO:Y or the amino acid sequence encoded by the cDNA in Clone ID NO:Z; (g) a nucleotide sequence encoding a biologically active fragment of an ovarian associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (h) a nucleotide sequence encoding an antigenic fragment of an ovarian associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; and (i) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), or (h), above.

[0075] The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), or (i) above, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the cDNA contained in Clone ID NO:Z or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA contained in Clone ID NO:Z, the nucleotide coding sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, a nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, the nucleotide sequence in SEQ ID NO:X encoding the polypeptide sequence as defined in column 6 of Table 1 or the complementary strand thereto, nucleotide sequences encoding a polypeptide as defined in column 6 of Table 1 or the complementary strand thereto, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides and nucleic acids.

[0076] In a preferred embodiment, the invention encompasses nucleic acid molecules which comprise, or alternatively, consist of a polynucleotide which hybridizes under stringent hybridization conditions, or alternatively, under lower stringency conditions, to a polynucleotide in (a), (b), (c), (d), (e), (f), (g), (h), or (i) above, as are polypeptides encoded by these polynucleotides. In another preferred embodiment, polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.



[0077] In another embodiment, the invention provides a purified protein comprising, or alternatively consisting of, a polypeptide having an amino acid sequence selected from the group consisting of: (a) the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (b) the amino acid sequence of a mature ovarian associated polypeptide having the amino acid sequence of SEQ ID NO:Y or the amino acid sequence encoded by the cDNA in Clone ID NO:Z; (c) the amino acid sequence of a biologically active fragment of an ovarian associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; and (d) the amino acid sequence of an antigenic fragment of an ovarian associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z.

[0078] The present invention is also directed to proteins which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the amino acid sequences in (a), (b), (c), or (d), above, the amino acid sequence shown in SEQ ID NO:Y, the amino acid sequence encoded by the cDNA contained in Clone ID NO:Z, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2, the amino acid sequence as defined in column 6 of Table 1, an amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X, and an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X. Fragments of these polypeptides are also provided (e.g., those fragments described herein). Further proteins encoded by polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these amino acid sequences under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are the polynucleotides encoding these proteins.

[0079] By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100

nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence referred to in Table 1 or 2 as the ORF (open reading frame), or any fragment specified, as described herein.

[0080] As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is expressed as percent-identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

[0081] If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to

arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

[0082] For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

[0083] By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

[0084] As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence of a polypeptide referred to in Table 1 (e.g., an amino acid sequence identified in columns 5 or 6) or Table 2 (e.g., the amino acid sequence of the polypeptide encoded by the polynucleotide sequence defined in columns 8 and 9 of Table 2) or a fragment thereof, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or an amino acid sequence of the polypeptide encoded by cDNA contained in Clone ID NO:Z, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237-245 (1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

[0085] If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the

present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C- terminal residues of the subject sequence.

[0086] For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

[0087] The polynucleotide variants of the invention may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, polypeptide variants in which less than 50, less than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

[0088] Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

[0089] Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptides of the present invention without substantial loss of biological function. As an example, the authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

[0090] Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem. 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

[0091] Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are

removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

[0092] Thus, the invention further includes polypeptide variants which show a functional activity (e.g., biological activity) of the polypeptides of the invention. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as to have little effect on activity.

[0093] The present application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, (e.g., encoding a polypeptide having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having functional activity include, *inter alia*, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) *in situ* hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); (3) Northern Blot analysis for detecting mRNA expression in specific tissues (e.g., normal ovarian tissues or diseased ovarian tissues); and (4) *in situ* hybridization (e.g., histochemistry) for detecting mRNA expression in specific tissues (e.g., normal ovarian tissues or diseased ovarian tissues).

[0094] Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, which do, in fact, encode a polypeptide having functional activity. By a polypeptide having "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide of the

invention for binding) to an anti-polypeptide of the invention antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention.

[0095] The functional activity of the polypeptides, and fragments, variants and derivatives of the invention, can be assayed by various methods.

[0096] For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the present invention for binding to an anti-polypeptide of the invention antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

[0097] In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, the ability of physiological correlates of a polypeptide of the present invention to bind to a substrate(s) of the polypeptide of the invention can be routinely assayed using techniques known in the art.

[0098] In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present



invention and fragments, variants and derivatives thereof to elicit polypeptide related biological activity (either *in vitro* or *in vivo*). Other methods will be known to the skilled artisan and are within the scope of the invention.

[0100] Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA contained in Clone ID NO:Z, a nucleic acid sequence referred to in Table 1 (e.g., SEQ ID NO:X), a nucleic acid sequence disclosed in Table 2 (e.g., the nucleic acid sequence delineated in columns 8 and 9) or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

[0101] For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," *Science* 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

[0102] The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

[0103] The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. See Cunningham et al., Science 244:1081-1085 (1989). The resulting mutant molecules can then be tested for biological activity.

[0104] As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly. Besides conservative amino acid substitutions, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitutions with one or more of the amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, serum albumin (preferably human serum albumin) or a fragment or variant thereof, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

[0105] For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical

formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. See Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).

[0106] A further embodiment of the invention relates to polypeptides which comprise the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions from a polypeptide sequence disclosed herein. Of course it is highly preferable for a polypeptide to have an amino acid sequence which comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, an amino acid sequence encoded by the complement of SEQ ID NO:X, and/or the amino acid sequence encoded by cDNA contained in Clone ID NO:Z which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions.

[0107] In specific embodiments, the polypeptides of the invention comprise, or alternatively, consist of, fragments or variants of a reference amino acid sequence selected from: (a) the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein); (b) the amino acid sequence encoded by SEQ ID NO:X or fragments thereof; (c) the amino acid sequence encoded by the complement of SEQ ID NO:X or fragments thereof; (d) the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or fragments thereof; and (e) the amino acid sequence encoded by cDNA contained in Clone ID NO:Z or fragments thereof; wherein the fragments or variants have 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, amino acid residue additions, substitutions, and/or deletions when compared to the reference amino acid sequence. In preferred embodiments, the amino acid substitutions are conservative. Polynucleotides encoding these polypeptides are also encompassed by the invention.

*Polynucleotide and Polypeptide Fragments*

[0108] The present invention is also directed to polynucleotide fragments of the polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers to a polynucleotide having a nucleic acid sequence which, for example: is a portion of the cDNA contained in Clone ID NO:Z or the complementary strand thereto; is a portion of the polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in Clone ID NO:Z or the complementary strand thereto; is a portion of a polynucleotide sequence encoding the amino acid sequence encoded by the region of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence in SEQ ID NO:X or the complementary strand thereto; is a polynucleotide sequence encoding a portion of the polypeptide of SEQ ID NO:Y; is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X; or is a polynucleotide sequence encoding a portion of a polypeptide encoded by the complement of the polynucleotide sequence in SEQ ID NO:X.

[0109] The polynucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in Clone ID NO:Z, or the nucleotide sequence shown in SEQ ID NO:X or the complementary strand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 160, 170, 180, 190, 200, 250, 500, 600, 1000, or 2000 nucleotides in length) are also encompassed by the invention.

[0110] Moreover, representative examples of polynucleotide fragments of the invention, comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500,

501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of SEQ ID NO:X, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[0111] Further representative examples of polynucleotide fragments of the invention, comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-

1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of the cDNA sequence contained in Clone ID NO:Z, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[0112] In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y, a portion of an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, a portion of an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, and/or a portion of an amino acid sequence

encoded by the cDNA contained in Clone ID NO:Z. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region. In a preferred embodiment, polypeptide fragments of the invention include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

[0113] Even if deletion of one or more amino acids from the N-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the N-terminus. Whether a particular polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted N-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

[0114] Accordingly, polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions is preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

[0115] The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X or the complement thereof, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or a polypeptide encoded by the cDNA contained in Clone ID NO:Z). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y, or the polypeptide encoded by



the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), and m is defined as any integer ranging from 2 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0116] The present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or a polypeptide encoded by the cDNA contained in Clone ID NO:Z). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and where n corresponds to the position of amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0117] In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), the cDNA contained in Clone ID NO:Z, and/or the complement thereof, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0118] Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example the ability of the shortened mutin to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutin with a

large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

[0119] The present application is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein. In preferred embodiments, the application is directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0120] Any polypeptide sequence encoded by, for example, the polynucleotide sequences set forth as SEQ ID NO:X or the complement thereof, (presented, for example, in Tables 1A and 2), or the cDNA contained in Clone ID NO:Z, may be analyzed to determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide encoded by a polynucleotide sequence of SEQ ID NO:X (e.g., the polypeptide of SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2) or the cDNA contained in Clone ID NO:Z may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; <http://www.dnastar.com/>).

[0121] Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions; Chou-Fasman alpha-regions, beta-regions, and turn-regions; Kyte-Doolittle hydrophilic regions and hydrophobic regions; Eisenberg alpha- and beta-amphipathic regions; Karplus-Schulz flexible regions; Emini surface-forming regions; and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.

[0122] Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e.,

containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

[0123] Preferred polypeptide fragments of the invention are fragments comprising, or alternatively, consisting of, an amino acid sequence that displays a functional activity (e.g. biological activity) of the polypeptide sequence of which the amino acid sequence is a fragment. By a polypeptide displaying a "functional activity" is meant a polypeptide capable of one or more known functional activities associated with a full-length protein, such as, for example, biological activity, antigenicity, immunogenicity, and/or multimerization, as described herein.

[0124] Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased-undesirable activity.

[0125] In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of SEQ ID NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0126] The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of: the polypeptide sequence shown in SEQ ID NO:Y; a polypeptide sequence encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2; the polypeptide sequence encoded by the cDNA contained in Clone ID NO:Z; or the polypeptide sequence encoded by a polynucleotide that hybridizes to the sequence of SEQ ID NO:X, the complement of the sequence of SEQ ID NO:X, the complement of a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, or

the cDNA sequence contained in Clone ID NO:Z under stringent hybridization conditions or alternatively, under lower stringency hybridization as defined *supra*. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X, or a fragment thereof), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to the complementary strand under stringent hybridization conditions or alternatively, under lower stringency hybridization conditions defined *supra*.

[0127] The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described *infra*. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998-4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross-reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

[0128] Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

[0129] In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid

residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

[0130] Non-limiting examples of epitopes of polypeptides that can be used to generate antibodies of the invention include a polypeptide comprising, or alternatively consisting of, at least one, two, three, four, five, six or more of the portion(s) of SEQ ID NO:Y specified in column 6 of Table 1. These polypeptide fragments have been determined to bear antigenic epitopes of the proteins of the invention by the analysis of the Jameson-Wolf antigenic index which is included in the DNASTar suite of computer programs. By "comprise" it is intended that a polypeptide contains at least one, two, three, four, five, six or more of the portion(s) of SEQ ID NO:Y shown in column 6 of Table 1, but it may contain additional flanking residues on either the amino or carboxyl termini of the recited portion. Such additional flanking sequences are preferably sequences naturally found adjacent to the portion; i.e., contiguous sequence shown in SEQ ID NO:Y. The flanking sequence may, however, be sequences from a heterologous polypeptide, such as from another protein described herein or from a heterologous polypeptide not described herein. In particular embodiments, epitope portions of a polypeptide of the invention comprise one, two, three, or more of the portions of SEQ ID NO:Y shown in column 6 of Table 1. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0131] Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. See, for instance, Sutcliffe et al., *supra*; Wilson et al., *supra*; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one

or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

[0132] Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, *in vivo* immunization, *in vitro* immunization, and phage display methods. See, e.g., Sutcliffe et al., *supra*; Wilson et al., *supra*, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If *in vivo* immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

[0133] As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention (e.g., those comprising an immunogenic or antigenic epitope) can be fused to heterologous polypeptide sequences. For example, polypeptides of the present invention (including fragments or variants thereof), may be fused with the

constant domain of immunoglobulins (IgG, IgM, or IgA), or portions thereof (CH1, CH2, CH3, or any combination thereof), resulting in chimeric polypeptides. By way of another non-limiting example, polypeptides and/or antibodies of the present invention (including fragments thereof) may be fused with albumin (including but not limited to recombinant human albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,962, 1992, 1992, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 9, 1999, incorporated by reference in their entirety)). In a preferred embodiment, antibodies of the present invention (including fragments or variants thereof) fused with the mature form of human serum albumin (i.e., amino acids 1-585 of human serum albumin as shown in Figures 1 and 2 of EP Patent 0 322 094) is incorporated by reference in its entirety. In another preferred embodiment, antibodies of the present invention (including fragments or variants thereof) fused with polypeptide fragments comprising, or alternatively consisting of, residues 1-z of human serum albumin, where z is an integer from 1 to 585, are incorporated by reference in its entirety. Polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused to either the N- or C-terminal end of the heterologous polypeptide or human serum albumin polypeptide. Coding fusion proteins of the invention are also encompassed by the invention.

[0134] Such fusion proteins as described above may facilitate purification and may increase half-life *in vivo*. This has been shown for chimeric proteins consisting of the first two domains of the human IgG1 and various domains of the constant regions of the heavy or light chain of immunoglobulins. See, e.g., EP 394,827; Traunecker et al., *Nature*, 1-888, 1988. Enhanced delivery of an antigen across the epithelial barrier to the lymphatic system has been demonstrated for antigens (e.g., insulin) conjugated to an Fc dimer such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024/O813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to disulfide bonds have also been found to be more efficient in internalizing other molecules than monomeric polypeptides or fragments thereof, e.g., Fountoulakis et al., J.

Biochem., 270:3958-3964 (1995). Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin (HA) tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., 1991, Proc. Natl. Acad. Sci. USA 88:8972- 897). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni<sup>2+</sup> nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

#### *Fusion Proteins*

[0135] Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

[0136] Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

[0137] In certain preferred embodiments, proteins of the invention are fusion proteins comprising an amino acid sequence that is an N and/or C- terminal deletion of a polypeptide of the invention. In preferred embodiments, the invention is directed to a fusion protein comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence of the invention. Polynucleotides encoding these proteins are also encompassed by the invention.



[0138] Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

[0139] As one of skill in the art will appreciate that, as discussed above, polypeptides of the present invention, and epitope-bearing fragments thereof, can be combined with heterologous polypeptide sequences. For example, the polypeptides of the present invention may be fused with heterologous polypeptide sequences, for example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM) or portions thereof (CH1, CH2, CH3, and any combination thereof, including both entire domains and portions thereof), or albumin (including, but not limited to, native or recombinant human albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)), resulting in chimeric polypeptides. For example, EP-A-O-464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties (EP-A 0232 262). Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. See, D. Bennett et al., *J. Molecular Recognition* 8:52-58 (1995); K. Johanson et al., *J. Biol. Chem.* 270:9459-9471 (1995).

[0140] Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a polypeptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984).)

[0141] Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"), briefly described below, and further described herein. DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308-13 (1998); each of these patents and publications are hereby incorporated by reference in its entirety. In a preferred embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc., of one or more heterologous molecules encoding a heterologous polypeptide.

[0142] Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

#### **Recombinant and Synthetic Production of Polypeptides of the Invention**

[0143] The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by synthetic and recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or

retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

[0144] The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged *in vitro* using an appropriate packaging cell line and then transduced into host cells.

[0145] The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the *E. coli lac*, *trp*, *phoA* and *tac* promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

[0146] As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance, glutamine synthase, for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in *E. coli* and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells (e.g., *Saccharomyces cerevisiae* or *Pichia pastoris* (ATCC Accession No. 201178)); insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, 293, NSO and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

[0147] Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG

available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlsbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.

[0148] Vectors which use glutamine synthase (GS) or DHFR as the selectable markers can be amplified in the presence of the drugs methionine sulfoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors is the availability of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine synthase negative. Glutamine synthase expression systems can also function in glutamine synthase expressing cells (e.g., Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657 which are hereby incorporated in their entireties by reference herein. Additionally, glutamine synthase expression vectors can be obtained from Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in Bebbington et al., *Bio/technology* 10:169(1992) and in Biblia and Robinson *Biotechnol. Prog.* 11:1 (1995) which are herein incorporated by reference.

[0149] The present invention also relates to host cells containing the above-described vector constructs described herein, and additionally encompasses host cells containing nucleotide sequences of the invention that are operably associated with one or more heterologous control regions (e.g., promoter and/or enhancer) using techniques known of in the art. The host cell can be a higher eukaryotic cell, such as a mammalian cell (e.g., a human derived cell), or a lower eukaryotic cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. A host strain may be chosen which modulates the expression of the inserted gene sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically engineered

polypeptide may be controlled. Furthermore, different host cells have characteristics and specific mechanisms for the translational and post-translational processing and modification (e.g., phosphorylation, cleavage) of proteins. Appropriate cell lines can be chosen to ensure the desired modifications and processing of the foreign protein expressed.

[0150] Introduction of the nucleic acids and nucleic acid constructs of the invention into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

[0151] In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., ovarian antigen coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with ovarian associated polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous ovarian associated polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous ovarian associated polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent Number 5,641,670, issued June 24, 1997; International Publication Number WO 96/29411; International Publication Number WO 94/12650; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

[0152] Polypeptides of the present invention can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host

employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

[0153] In one embodiment, the yeast *Pichia pastoris* is used to express polypeptides of the invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A main step in the methanol metabolism pathway is the oxidation of methanol to formaldehyde using O<sub>2</sub>. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O<sub>2</sub>. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOX1*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOX1* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. See, Ellis, S.B., *et al.*, *Mol. Cell. Biol.* 5:1111-21 (1985); Koutz, P.J., *et al.*, *Yeast* 5:167-77 (1989); Tschopp, J.F., *et al.*, *Nucl. Acids Res.* 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the *AOX1* regulatory sequence is expressed at exceptionally high levels in *Pichia* yeast grown in the presence of methanol.

[0154] In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector

allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

[0155] Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYDI, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

[0156] In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

[0157] In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

[0158] In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, Proteins: Structures and

Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., *Nature*, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid,  $\alpha$ -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid,  $\gamma$ -Abu,  $\epsilon$ -Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine,  $\beta$ -alanine, fluoro-amino acids, designer amino acids such as  $\beta$ -methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

[0159] The invention encompasses polypeptides of the present invention which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease,  $\text{NaBH}_4$ ; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

[0160] Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label; such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

[0161] Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic



group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include iodine ( $^{121}\text{I}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{111}\text{In}$ ,  $^{112}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{115\text{m}}\text{In}$ ), technetium ( $^{99}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ), thallium ( $^{201}\text{Tl}$ ), gallium ( $^{68}\text{Ga}$ ,  $^{67}\text{Ga}$ ), palladium ( $^{103}\text{Pd}$ ), molybdenum ( $^{99}\text{Mo}$ ), xenon ( $^{133}\text{Xe}$ ), fluorine ( $^{18}\text{F}$ ),  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ ,  $^{159}\text{Gd}$ ,  $^{149}\text{Pm}$ ,  $^{140}\text{La}$ ,  $^{175}\text{Yb}$ ,  $^{166}\text{Ho}$ ,  $^{90}\text{Y}$ ,  $^{47}\text{Sc}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{142}\text{Pr}$ ,  $^{105}\text{Rh}$ , and  $^{97}\text{Ru}$ .

[0162] In specific embodiments, a polypeptide of the present invention or fragment or variant thereof is attached to macrocyclic chelators that associate with radiometal ions, including but not limited to,  $^{177}\text{Lu}$ ,  $^{90}\text{Y}$ ,  $^{166}\text{Ho}$ , and  $^{153}\text{Sm}$ , to polypeptides. In a preferred embodiment, the radiometal ion associated with the macrocyclic chelators is  $^{111}\text{In}$ . In another preferred embodiment, the radiometal ion associated with the macrocyclic chelator is  $^{90}\text{Y}$ . In specific embodiments, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA). In other specific embodiments, DOTA is attached to an antibody of the invention or fragment thereof via a linker molecule. Examples of linker molecules useful for conjugating DOTA to a polypeptide are commonly known in the art - see, for example, DeNardo et al., Clin Cancer Res. 4(10):2483-90 (1998); Peterson et al., Bioconjug. Chem. 10(4):553-7 (1999); and Zimmerman et al, Nucl. Med. Biol. 26(8):943-50 (1999); which are hereby incorporated by reference in their entirety.

[0163] As mentioned, the ovarian associated proteins of the invention may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given ovarian associated polypeptide. Ovarian associated polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic ovarian associated polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent

attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth. Enzymol. 182:626-646 (1990); Rattan et al., Ann. N.Y. Acad. Sci. 663:48-62 (1992)).

[0164] Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

[0165] The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example,

the polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa.

[0166] As noted above, the polyethylene glycol may have a branched structure. Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo et al., *Appl. Biochem. Biotechnol.* 56:59-72 (1996); Vorobjev et al., *Nucleosides Nucleotides* 18:2745-2750 (1999); and Caliceti et al., *Bioconjug. Chem.* 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

[0167] The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, such as, for example, the method disclosed in EP 0 401 384 (coupling PEG to G-CSF), herein incorporated by reference; see also Malik et al., *Exp. Hematol.* 20:1028-1035 (1992), reporting pegylation of GM-CSF using tresyl chloride. For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

[0168] As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue

(e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

[0169] One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

[0170] As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either directly or by an intervening linker. Linkerless systems for attaching polyethylene glycol to proteins are described in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992); Francis et al., Intern. J. of Hematol. 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.

[0171] One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride ( $\text{ClSO}_2\text{CH}_2\text{CF}_3$ ). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoroethane sulphonyl group.

[0172] Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number of additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in International Publication No. WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

[0173] The number of polyethylene glycol moieties attached to each protein of the invention (i.e., the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado et al., *Crit. Rev. Thera. Drug Carrier Sys.* 9:249-304 (1992).

[0174] The ovarian associated polypeptides of the invention can be recovered and purified from chemical synthesis and recombinant cell cultures by standard methods which include, but are not limited to, ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification. Well known techniques for refolding protein may be employed to regenerate active conformation when the polypeptide is denatured during isolation and/or purification.

[0175] Ovarian associated polynucleotides and polypeptides may be used in

accordance with the present invention for a variety of applications, particularly those that make use of the chemical and biological properties of ovarian associated antigens. Among these are applications in the detection, prevention, diagnosis and/or treatment of diseases associated with the ovaries and/or breast; such as e.g., ovarian and/or breast cancer and tumors (e.g., ovarian Krukenberg tumor, malignant mixed Mullerian tumors, and/or as described under "Hyperproliferative Disorders" below), infectious diseases (e.g., mastitis, oophoritis, and/or as described under "Infectious Diseases" below), and inflammatory diseases (e.g., abscesses and/or as described under "Immune Disorders" below), and as described under "Reproductive System Disorders" below. Additional applications relate to diagnosis and to treatment of disorders of cells, tissues and organisms. These aspects of the invention are discussed further below.

[0176] In a preferred embodiment, polynucleotides expressed in a particular tissue type (see, e.g., Table 1, column 7) are used to detect, diagnose, treat, prevent and/or prognose disorders associated with the tissue type.

[0177] The polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

[0178] Multimers encompassed by the invention may be homomers or heteromers. As used herein, the term homomer refers to a multimer containing only polypeptides corresponding to a protein of the invention (e.g., the amino acid sequence of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X or the complement of SEQ ID NO:X, the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or an amino acid sequence encoded by cDNA contained in Clone ID NO:Z (including fragments, variants, splice variants, and fusion proteins, corresponding to these as described herein)). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid

sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (e.g., containing two polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing three polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

[0179] As used herein, the term heteromer refers to a multimer containing two or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

[0180] Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked by, for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or encoded by the cDNA contained in Clone ID NO:Z). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide

sequence in a fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., U.S. Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for example, osteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

[0181] Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

[0182] Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by



reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

[0183] In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention containing Flag® polypeptide sequence. In a further embodiment, proteins of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

[0184] The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide components desired to be contained in the multimer of the invention (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

[0185] Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a

linker polypeptide and then further to a synthetic polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hydrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

### **Antibodies**

[0186] Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of the invention (e.g., a polypeptide or fragment or variant of the amino acid sequence of SEQ ID NO:Y or a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or an epitope, of the present invention) as determined by immunoassays well known in the art for assaying specific antibody-antigen binding. Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), intracellularly-made antibodies (i.e., intrabodies), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. In preferred embodiments, the immunoglobulin molecules of the invention are IgG1. In other preferred embodiments, the immunoglobulin molecules of the invention are IgG4.

[0187] Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')<sub>2</sub>, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, sheep rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described *infra* and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

[0188] The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

[0189] Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues, or listed in the Tables and Figures. Preferred epitopes of the invention include those shown in column 6 of Table 1, as well as polynucleotides that encode these epitopes. Antibodies which specifically bind any epitope or polypeptide of

the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

[0190] Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-2}$  M,  $10^{-2}$  M,  $5 \times 10^{-3}$  M,  $10^{-3}$  M,  $5 \times 10^{-4}$  M,  $10^{-4}$  M,  $5 \times 10^{-5}$  M,  $10^{-5}$  M,  $5 \times 10^{-6}$  M,  $10^{-6}$  M,  $5 \times 10^{-7}$  M,  $10^{-7}$  M,  $5 \times 10^{-8}$  M,  $10^{-8}$  M,  $5 \times 10^{-9}$  M,  $10^{-9}$  M,  $5 \times 10^{-10}$  M,  $10^{-10}$  M,  $5 \times 10^{-11}$  M,  $10^{-11}$  M,  $5 \times 10^{-12}$  M,  $10^{-12}$  M,  $5 \times 10^{-13}$  M,  $10^{-13}$  M,  $5 \times 10^{-14}$  M,  $10^{-14}$  M,  $5 \times 10^{-15}$  M, or  $10^{-15}$  M.

[0191] The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein.

In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85 %, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

[0192] Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described *supra*). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

[0193] The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT

publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res. 58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

[0194] Antibodies of the present invention may be used, for example, to purify, detect, and target the polypeptides of the present invention, including both *in vitro* and *in vivo* diagnostic and therapeutic methods. For example, the antibodies have utility in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); incorporated by reference herein in its entirety.

[0195] As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalent and non-covalent conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins: See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387; the disclosures of which are incorporated herein by reference in their entireties.

[0196] The antibodies of the invention include derivatives that are modified, i.e., by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation,

amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

[0197] The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of-interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

[0198] Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

[0199] Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non-limiting example, mice can be immunized with a polypeptide of

the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

[0200] Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

[0201] Another well known method for producing both polyclonal and monoclonal human B cell lines is transformation using Epstein Barr Virus (EBV). Protocols for generating EBV-transformed B cell lines are commonly known in the art, such as, for example, the protocol outlined in Chapter 7.22 of Current Protocols in Immunology, Coligan et al., Eds., 1994, John Wiley & Sons, NY, which is hereby incorporated in its entirety by reference herein. The source of B cells for transformation is commonly human peripheral blood, but B cells for transformation may also be derived from other sources including, but not limited to, lymph nodes, tonsil, spleen, tumor tissue, and infected tissues. Tissues are generally made into single cell suspensions prior to EBV transformation. Additionally, steps may be taken to either physically remove or inactivate T cells (e.g., by treatment with cyclosporin A) in B cell-containing samples, because T cells from individuals seropositive for anti-EBV antibodies can suppress B cell immortalization by EBV.

[0202] In general, the sample containing human B cells is innoculated with EBV, and cultured for 3-4 weeks. A typical source of EBV is the culture supernatant of the B95-



8 cell line (ATCC #VR-1492). Physical signs of EBV transformation can generally be seen towards the end of the 3-4 week culture period. By phase-contrast microscopy, transformed cells may appear large, clear, hairy and tend to aggregate in tight clusters of cells. Initially, EBV lines are generally polyclonal. However, over prolonged periods of cell cultures, EBV lines may become monoclonal or polyclonal as a result of the selective outgrowth of particular B cell clones. Alternatively, polyclonal EBV transformed lines may be subcloned (e.g., by limiting dilution culture) or fused with a suitable fusion partner and plated at limiting dilution to obtain monoclonal B cell lines. Suitable fusion partners for EBV transformed cell lines include mouse myeloma cell lines (e.g., SP2/0, X63-Ag8.653), heteromyeloma cell lines (human x mouse; e.g., SPAM-8, SBC-H20, and CB-F7), and human cell lines (e.g., GM 1500, SKO-007, RPMI 8226, and KR-4). Thus, the present invention also provides a method of generating polyclonal or monoclonal human antibodies against polypeptides of the invention or fragments thereof, comprising EBV-transformation of human B cells.

[0203] Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')<sub>2</sub> fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')<sub>2</sub> fragments). F(ab')<sub>2</sub> fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain. For example, the antibodies of the present invention can also be generated using various phage display methods known in the art and as discussed in detail in the Examples (e.g., Example 10). In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be

used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

[0204] As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')<sub>2</sub> fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

[0205] Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999 (1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including *in vivo* use of antibodies in humans and *in vitro* detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their

entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

[0206] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

[0207] Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and

light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, *Int. Rev. Immunol.* 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; 5,939,598; 6,075,181 and 6,114,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

[0208] Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., *Bio/technology* 12:899-903 (1988)).

[0209] Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotypic antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona,

FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand/receptor. For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby block its biological activity. Alternatively, antibodies which bind to and enhance polypeptide multimerization and/or binding, and/or receptor/ligand multimerization, binding and/or signaling can be used to generate anti-idiotypes that function as agonists of a polypeptide of the invention and/or its ligand/receptor. Such agonistic anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens as agonists of the polypeptides of the invention or its ligand(s)/receptor(s). For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby promote or enhance its biological activity.

[0210] Intrabodies of the invention can be produced using methods known in the art, such as those disclosed and reviewed in Chen et al., Hum. Gene Ther. 5:595-601 (1994); Marasco, W.A., Gene Ther. 4:11-15 (1997); Rondon and Marasco, Annu. Rev. Microbiol. 51:257-283 (1997); Proba et al., J. Mol. Biol. 275:245-253 (1998); Cohen et al., Oncogene 17:2445-2456 (1998); Ohage and Steipe, J. Mol. Biol. 291:1119-1128 (1999); Ohage et al., J. Mol. Biol. 291:1129-1134 (1999); Wirtz and Steipe, Protein Sci. 8:2245-2250 (1999); Zhu et al., J. Immunol. Methods 231:207-222 (1999); and references cited therein.

#### *Polynucleotides Encoding Antibodies*

[0211] The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined *supra*, to polynucleotides that encode

an antibody, preferably, that encodes a peptide of the invention, preferably, an antibody that has an amino acid sequence of SEQ ID NO:Y, to a polypeptide of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and a cDNA contained in Clone ID NO:Z.

[0212] The polynucleotide sequence of the polynucleotides determined, by the art. For example, if the nucleotide sequence of the antisense encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., BioTechniques 20, 1100-1104, involves the synthesis of overlapping oligonucleotides encoding the antibody, annealing and ligation of those oligonucleotides followed by PCR amplification of the ligated oligonucleotides by PCR.

[0213] Alternatively, a cDNA encoding an antibody may be generated from nucleic acid from a suitable source if a nucleic acid encoding a particular antibody is not available when the antibody molecule is known, a nucleic acid encoding the antibody synthesized or obtained from a suitable source (e.g., an antibody library generated from, or nucleic acid, preferably poly A nucleic acid or cells expressing the antibody, such as hybridoma cells secreting antibody of the invention) by PCR amplification using synthetic primers at the 3' and 5' ends of the sequence or by cloning using a restriction enzyme for the particular gene sequence to identify, e.g., a cDNA that encodes the antibody. Amplified nucleic acids generated into replicable cloning vectors using any method well known.

[0214] Once the nucleotide sequence of the amino acid sequence of the antibody is determined, the antibody may be manipulated using methods well known in the art for nucleotide sequences, e.g., recombinant DNA techniques, etc. (see, for example, the techniques described in Sambrook, et al., Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press and Ausubel et al., eds.,

1998, Current Protocols in Molecular Biology, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties ), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

[0215] In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well known in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human antibody, as described *supra*. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed *supra*, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

[0216] In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described *supra*, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

[0217] Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423- 42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in *E. coli* may also be used (Skerra et al., Science 242:1038- 1041 (1988)).

#### *Methods of Producing Antibodies*

[0218] The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques. Methods of producing antibodies include, but are not limited to, hybridoma technology, EBV transformation, and other methods discussed herein as well as through the use recombinant DNA technology, as discussed below.

[0219] Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the



antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

[0220] The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

[0221] A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., *E. coli*, *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., *Saccharomyces*, *Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as *Escherichia coli*, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example,

mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., Gene 45:101 (1986); Cockett et al., Bio/Technology 8:2 (1990)).

[0222] In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., EMBO J. 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, Nucleic Acids Res. 13:3101-3109 (1985); Van Heeke & Schuster, J. Biol. Chem. 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

[0223] In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

[0224] In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result

in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

[0225] In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

[0226] For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in

the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

[0227] A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgp<sup>rt</sup>- or ap<sup>rt</sup>- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 (Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); TIB TECH 11(5):155-215 (1993)); and hyg<sup>ro</sup>, which confers resistance to hygromycin (Santerre et al., Gene 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., J. Mol. Biol. 150:1 (1981), which are incorporated by reference herein in their entireties.

[0228] The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA

cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., Mol. Cell. Biol. 3:257 (1983)).

[0229] Vectors which use glutamine synthase (GS) or DHFR as the selectable markers can be amplified in the presence of the drugs methionine sulfoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors are the availability of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine synthase negative. Glutamine synthase expression systems can also function in glutamine synthase expressing cells (e.g., Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657 which are incorporated in their entireties by reference herein. Additionally, glutamine synthase expression vectors that may be used according to the present invention are commercially available from suppliers, including, for example Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in Bebbington et al., Bio/technology 10:169(1992) and in Biblia and Robinson Biotechnol. Prog. 11:1 (1995) which are incorporated in their entireties by reference herein.

[0230] The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

[0231] Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide sequences described herein or otherwise known in the art, to facilitate purification.

[0232] The present invention encompasses antibodies recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either *in vitro* or *in vivo*, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in *in vitro* immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., *supra*, and PCT publication WO 93/21232; EP 439,095; Naramura et al., *Immunol. Lett.* 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., *PNAS* 89:1428-1432 (1992); Fell et al., *J. Immunol.* 146:2446-2452 (1991), which are incorporated by reference in their entireties.

[0233] The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or any combination of whole domains or

portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991); Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337-11341 (1992) (said references incorporated by reference in their entireties).

[0234] As discussed, *supra*, the polypeptides corresponding to a polypeptide, polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the *in vivo* half life of the polypeptides or for use in immunoassays using methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See EP 394,827; Traunecker et al., Nature 331:84-86 (1988). The polypeptides of the present invention fused or conjugated to an antibody having disulfide-linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. See, for example, Fountoulakis et al., J. Biochem. 270:3958-3964 (1995). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. See, for example, EP A 232,262. Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., J.

Molecular Recognition 8:52-58 (1995); Johanson et al., J. Biol. Chem. 270:9459-9471 (1995)).

[0235] Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the "HA" tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)) and the "flag" tag.

[0236] The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention.

[0237] Further, an antibody or fragment thereof may be conjugated to a therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example,  $^{213}\text{Bi}$ . A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin,



dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa, chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

[0238] The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor,  $\alpha$ -interferon,  $\beta$ -interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF- $\alpha$ , TNF- $\beta$ , AIM I (See, International Publication No. WO 97/33899), AIM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi *et al.*, *Int. Immunol.*, 6:1567-1574 (1994)), VEGI (See, International Publication No. WO 99/23105), a thrombotic agent or an anti-angiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

[0239] Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

[0240] Techniques for conjugating such therapeutic moiety to antibodies are well known. See, for example, Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of

Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev. 62:119-58 (1982).

[0241] Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

[0242] An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

#### *Immunophenotyping*

[0243] : The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. Translation products of the genes of the present invention may be useful as cell specific markers, or more specifically as cellular markers that are differentially expressed at various stages of differentiation and/or maturation of particular cell types. Monoclonal antibodies directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison et al., Cell, 96:737-49 (1999)).

[0244] These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease

(MRD) in acute leukemic patients) and "non-self" cells in transplantations to prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

#### *Assays For Antibody Binding*

[0245] The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, and protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

[0246] Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X- 100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasylol) supplemented with protein phosphatase and/or protease inhibitors (e.g., EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (e.g., 1-4 hours) at 4° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 4° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to immunoprecipitate a particular antigen can be assessed by, e.g., western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (e.g., pre-clearing the cell lysate with sepharose beads). For further discussion regarding immunoprecipitation protocols see, e.g., Ausubel et al., eds., (1994),

Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 10.16.1.

[0247] Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (e.g., 8%- 20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g.,  $^{32}\text{P}$  or  $^{125}\text{I}$ ) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al., eds., (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 10.8.1.

[0248] ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion

regarding ELISAs see, e.g., Ausubel et al., eds., (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 11.2.1.

[0249] The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g.,  $^3\text{H}$  or  $^{125}\text{I}$ ) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g.,  $^3\text{H}$  or  $^{125}\text{I}$ ) in the presence of increasing amounts of an unlabeled second antibody.

[0250] Antibodies of the invention may be characterized using immunocytochemistry methods on cells (e.g., mammalian cells, such as CHO cells) transfected with a vector enabling the expression of an ovarian antigen or with vector alone using techniques commonly known in the art. Antibodies that bind ovarian antigen transfected cells, but not vector-only transfected cells, are ovarian antigen specific.

#### *Therapeutic Uses*

[0251] The present invention is further directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions described herein. The treatment and/or prevention of diseases, disorders, or conditions associated with aberrant expression and/or activity of a

polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

[0252] In a specific and preferred embodiment, the present invention is directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the diseases, disorders, or conditions of the ovarian and/or breast, including, but not limited to, neoplastic disorders (e.g., ovarian Krukenberg tumor, malignant mixed Mullerian tumors, and/or as described under "Hyperproliferative Disorders" below), infectious diseases (e.g., mastitis, oophoritis, and/or as described under "Infectious Diseases" below), and inflammatory diseases (e.g., abscesses and/or as described under "Immune Disorders" below), and as described under "Reproductive System Disorders" below. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (e.g., antibodies directed to the full length protein expressed on the cell surface of a mammalian cell; antibodies directed to an epitope of an ovarian associated polypeptide of the invention (such as, a linear epitope (shown in Table 1, column 6) or a conformational epitope), including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions of the ovaries and/or breast described herein. The treatment and/or prevention of diseases, disorders, or conditions of the ovaries and/or breast associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

[0253] A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the

present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

[0254] The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

[0255] The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

[0256] It is preferred to use high affinity and/or potent *in vivo* inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-2}$  M,  $10^{-2}$  M,  $5 \times 10^{-3}$  M,  $10^{-3}$  M,  $5 \times 10^{-4}$  M,  $10^{-4}$  M,  $5 \times 10^{-5}$  M,  $10^{-5}$  M,  $5 \times 10^{-6}$  M,  $10^{-6}$  M,  $5 \times 10^{-7}$  M,  $10^{-7}$  M,  $5 \times 10^{-8}$  M,  $10^{-8}$  M,  $5 \times 10^{-9}$  M,  $10^{-9}$  M,  $5 \times 10^{-10}$  M,  $10^{-10}$  M,  $5 \times 10^{-11}$  M,  $10^{-11}$  M,  $5 \times 10^{-12}$  M,  $10^{-12}$  M,  $5 \times 10^{-13}$  M,  $10^{-13}$  M,  $5 \times 10^{-14}$  M,  $10^{-14}$  M,  $5 \times 10^{-15}$  M, and  $10^{-15}$  M.

[0257] In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

[0258] Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

[0259] For general reviews of the methods of gene therapy, see Goldspiel et al., *Clinical Pharmacy* 12:488-505 (1993); Wu and Wu, *Biotherapy* 3:87-95 (1991); Tolstoshev, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596 (1993); Mulligan, *Science* 260:926-932 (1993); and Morgan and Anderson, *Ann. Rev. Biochem.* 62:191-217 (1993); May, *TIBTECH* 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, NY (1993); and Kriegler, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY (1990).

[0260] In a preferred embodiment, the compound comprises nucleic acid sequences encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); Zijlstra et al., *Nature* 342:435-438 (1989). In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.



[0261] Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid- carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids *in vitro*, then transplanted into the patient. These two approaches are known, respectively, as *in vivo* or *ex vivo* gene therapy.

[0262] In a specific embodiment, the nucleic acid sequences are directly administered *in vivo*, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted *in vivo* for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

[0263] In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to

be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., *Biotherapy* 6:291-302 (1994), which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., *J. Clin. Invest.* 93:644-651 (1994); Kiem et al., *Blood* 83:1467-1473 (1994); Salmons and Gunzberg, *Human Gene Therapy* 4:129-141 (1993); and Grossman and Wilson, *Curr. Opin. in Genetics and Devel.* 3:110-114 (1993).

[0264] Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, *Current Opinion in Genetics and Development* 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., *Human Gene Therapy* 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., *Science* 252:431-434 (1991); Rosenfeld et al., *Cell* 68:143-155 (1992); Mastrangeli et al., *J. Clin. Invest.* 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., *Gene Therapy* 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

[0265] Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., *Proc. Soc. Exp. Biol. Med.* 204:289-300 (1993); U.S. Patent No. 5,436,146).

[0266] Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

[0267] In this embodiment, the nucleic acid is introduced into a cell prior to administration *in vivo* of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, Meth. Enzymol. 217:599-618 (1993); Cohen et al., Meth. Enzymol. 217:618-644 (1993); Cline, Pharmac. Ther. 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

[0268] The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

[0269] Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

[0270] In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

[0271] In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered *in vivo* for therapeutic effect. In a specific embodiment, stem or progenitor

cells are used. Any stem and/or progenitor cells which can be isolated and maintained *in vitro* can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, Cell 71:973-985 (1992); Rheinwald, Meth. Cell Bio. 21A:229 (1980); and Pittelkow and Scott, Mayo Clinic Proc. 61:771 (1986)).

[0272] In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by the presence or absence of an appropriate inducer of transcription.

#### *Demonstration of Therapeutic or Prophylactic Activity*

[0273] The compounds or pharmaceutical compositions of the invention are preferably tested *in vitro*, and then *in vivo* for the desired therapeutic or prophylactic activity, prior to use in humans. For example, *in vitro* assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, *in vitro* assays which can be used to determine whether administration of a specific compound is indicated, include *in vitro* cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

#### *Therapeutic/Prophylactic Administration and Composition*

[0274] The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical composition of the invention, preferably a polypeptide or antibody of the invention. In a preferred embodiment, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is

preferably an animal, including but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

[0275] Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or an immunoglobulin are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.

[0276] Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

[0277] In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when

administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.

[0278] In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

[0279] In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, *CRC Crit. Ref. Biomed. Eng.* 14:201 (1987); Buchwald et al., *Surgery* 88:507 (1980); Saudek et al., *N. Engl. J. Med.* 321:574 (1989)). In another embodiment, polymeric materials can be used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., *Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., *Science* 228:190 (1985); During et al., *Ann. Neurol.* 25:351 (1989); Howard et al., *J. Neurosurg.* 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, e.g., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

[0280] Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

[0281] In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered *in vivo* to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox- like peptide which is known to enter the nucleus (see e.g., Joliot et al., *Proc. Natl. Acad. Sci. USA* 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be

introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

[0282] The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

[0283] In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous

administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

[0284] The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

[0285] The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

[0286] For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies



and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

[0287] The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

#### *Diagnosis and Imaging*

[0288] Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, or monitor diseases, disorders, and/or conditions associated with the aberrant expression and/or activity of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of aberrant expression.

[0289] The invention provides a diagnostic assay for diagnosing an ovarian and/or breast disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of

actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

[0290] Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen et al., J. Cell Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine ( $^{125}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{112}\text{In}$ ), and technetium ( $^{99}\text{Tc}$ ); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0291] One facet of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most preferably a human. A preferred embodiment of the invention is the detection and diagnosis of a disease or disorder of the ovarian associated with aberrant expression of an ovarian antigen in an animal, preferably a mammal and most preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which specifically binds to the polypeptide of interest; b) waiting for a time interval following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for a particular system.

[0292] It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of <sup>99m</sup>Tc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

[0293] Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.

[0294] In an embodiment, the method for diagnosing the disease or disorder, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.

[0295] Presence of the labeled molecule can be detected in the patient using methods known in the art for *in vivo* scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.

[0296] In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patient using positron emission-tomography. In yet

another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

#### *Kits*

[0297] The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody included in the kit. Preferably, the kits of the present invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate).

[0298] In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react with the polypeptide of interest. Such a kit may include a substantially isolated polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

[0299] In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

[0300] In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific embodiment, the antibody may be a monoclonal antibody. The detecting means of the kit may include a second, labeled monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

[0301] In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

[0302] The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

[0303] Thus, the invention provides an assay system or kit for carrying out this diagnostic method. The kit generally includes a support with surface-bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

### Uses of the Polynucleotides

[0304] Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

[0305] The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome, thus each polynucleotide of the present invention can routinely be used as a chromosome marker using techniques known in the art. Table 1, column 8 provides the chromosome location of some of the polynucleotides of the invention.

[0306] Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably at least 15 bp (e.g., 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can optionally be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to SEQ ID NO:X will yield an amplified fragment.

[0307] Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries, and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety).

[0308] Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides

2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

[0309] For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

[0310] Thus, the present invention also provides a method for chromosomal localization which involves (a) preparing PCR primers from the polynucleotide sequences in Table 1 and/or Table 2 and SEQ ID NO:X and (b) screening somatic cell hybrids containing individual chromosomes.

[0311] The polynucleotides of the present invention would likewise be useful for radiation hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g. Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London (1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton et al., Methods Cell Biol. 62:265-280 (2000); and/or Ott, J. Hered. 90:68-70 (1999), each of which is hereby incorporated by reference in its entirety.

[0312] Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library).) Column 9 of Table 1 provides an OMIM reference identification number of diseases associated with the cytologic band disclosed in column 8 of Table 1, as determined using techniques described herein and by reference to Table 5. Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

[0313] Thus, once coinheritance is established, differences in a polynucleotide of the invention and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or

translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicate that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

[0314] Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using the polynucleotides of the invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker. Diagnostic and prognostic methods, kits and reagents encompassed by the present invention are briefly described below and more thoroughly elsewhere herein (see e.g., the sections labeled "Antibodies", "Diagnostic Assays", and "Methods for Detecting Ovarian and/or Breast Disease, Including Cancer").

[0315] Thus, the invention also provides a diagnostic method useful during diagnosis of a disorder, involving measuring the expression level of polynucleotides of the present invention in cells or body fluid from an individual and comparing the measured gene expression level with a standard level of polynucleotide expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a disorder. Additional non-limiting examples of diagnostic methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., Example 12).

[0316] In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject, as further described herein. In a general embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the invention, where each probe has one strand containing a 31'-mer-end internal to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.



[0317] Where a diagnosis of a related disorder, including, for example, diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed polynucleotide of the invention expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

[0318] By "measuring the expression level of polynucleotides of the invention" is intended qualitatively or quantitatively measuring or estimating the level of the polypeptide of the invention or the level of the mRNA encoding the polypeptide of the invention in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the polypeptide level or mRNA level in a second biological sample). Preferably, the polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the related disorder or being determined by averaging levels from a population of individuals not having a related disorder. As will be appreciated in the art, once a standard polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

[0319] By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains polypeptide of the present invention or the corresponding mRNA. As indicated, biological samples include body fluids (such as semen, lymph, vaginal pool, sera, plasma, urine, synovial fluid and spinal fluid) which contain the polypeptide of the present invention, and tissue sources found to express the polypeptide of the present invention. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

[0320] The method(s) provided above may preferably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides of the invention are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in U.S. Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with polynucleotides of the invention attached may be used to identify polymorphisms between the isolated polynucleotide sequences of the invention,

with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e., their location, as well as, their existence) would be beneficial in identifying disease loci for many disorders, such as for example, in neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, digestive disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions. Such a method is described in U.S. Patents 5,858,659 and 5,856,104. The U.S. Patents referenced *supra* are hereby incorporated by reference in their entirety herein.

[0321] The present invention encompasses polynucleotides of the present invention that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides of the invention are incorporated onto a solid support, or gene chip. For the purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by Nielsen et al., Science 254:1497 (1991); and Egholm et al., Nature 365:666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point ( $T_{sub.m}$ ) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15-mer duplex. Also, the absence of charge groups in PNA means that hybridization can be done at low ionic strengths and reduce possible interference by salt during the analysis.

[0322] The compounds of the present invention have uses which include, but are not limited to, detecting cancer in mammals. In particular the invention is useful during

diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia, acute myeloblastic leukemia, acute promyelocytic leukemia, acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

[0323] The compounds of the present invention have preferred uses which include, but are not limited to, detecting ovarian and/or breast cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: ovarian epithelial cancer, ovarian germ cell tumors, ovarian papillary serous adenocarcinoma, ovarian mucinous adenocarcinoma, ovarian Krukenberg tumor, malignant mixed Mullerian tumors, ovarian low malignant tumors, ductal carcinoma in situ, Paget's disease, lobular carcinoma in situ, invasive ductal carcinoma, invasive lobular carcinoma, medullary carcinoma, papillary carcinoma, secretory carcinoma, and apocrine carcinoma. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

[0324] Pathological cell proliferative disorders are often associated with inappropriate activation of proto-oncogenes. (Gelman, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in Neoplastic Diseases of the Blood, Vol 1., Wiernik, P. H. et al. eds., 161-182 (1985)). Neoplasias are now believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Gelman et al., *supra*) It is likely that mutated or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Gelman et al., *supra*) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Gelman et al., *supra*)

[0325] For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell line HL-60. When HL-60 cells are chemically induced to stop proliferation,

the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580). However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-myb blocks translation of the corresponding mRNAs which downregulates expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., Proc. Natl. Acad. Sci. 85:1028 (1988); Anfossi et al., Proc. Natl. Acad. Sci. 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness is not be limited to treatment, prevention, diagnosis and/or prognosis, of proliferative disorders of cells and tissues of hematopoietic origin, in light of the numerous cells and cell types of varying origins which are known to exhibit proliferative phenotypes. In preferred embodiments, the compounds and/or methods of the invention are used to treat, prevent, diagnose, and/or prognose, proliferative disorders of ovarian and/or breast cells and tissues.

[0326] In addition to the foregoing, a polynucleotide of the present invention can be used to control gene expression through triple helix formation or through antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. Neurochem. 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance Lee et al., Nucleic Acids Research 6: 3073 (1979); Cooney et al., Science 241: 456 (1988); and Dervan et al., Science 251: 1360 (1991). Both methods rely on binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. The oligonucleotide described above can also be delivered to cells such that the antisense RNA or DNA may be expressed *in vivo* to inhibit production of polypeptide of the present invention antigens. Both techniques are effective

in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease, and in particular, for the treatment of proliferative diseases and/or conditions. Non-limiting antisense and triple helix methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., the section labeled "Antisense and Ribozyme (Antagonists)").

[0327] Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell. Additional non-limiting examples of gene therapy methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., the sections labeled "Gene Therapy Methods" and Examples 16, 17 and 18).

[0328] The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

[0329] The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

[0330] Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant, urine, fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

[0331] There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers prepared from the sequences of the present invention, specific to tissues, including but not limited to, those sequences referred to in Table 1. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination. Additional non-limiting examples of such uses are further described herein.

[0332] Because ovarian antigens are found expressed in the ovaries, the polynucleotides of the present invention are also useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample. Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In a specific embodiment, the polynucleotides of the present invention are also useful as hybridization probes for differential identification of ovarian tissue(s) or cell type(s) present in a biological sample. Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of ovarian tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In addition, for a number of disorders of the

above tissues or cells, significantly higher or lower levels of gene expression of the polynucleotides/polypeptides of the present invention may be detected in certain tissues (e.g., tissues expressing polypeptides and/or polynucleotides of the present invention, for example, normal ovarian tissues or diseased ovarian tissues, and/or those tissues/cells corresponding to the library source relating to a polynucleotide sequence of the invention as disclosed in column 7 of Table 1, and/or cancerous and/or wounded tissues) or bodily fluids (e.g., semen, lymph, vaginal pool, serum, plasma, urine, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" gene expression level, i.e., the expression level in healthy tissue from an individual not having the disorder.

[0333] Thus, the invention provides a diagnostic method of a disorder, which involves: (a) assaying gene expression level in cells or body fluid of an individual; (b) comparing the gene expression level with a standard gene expression level, whereby an increase or decrease in the assayed gene expression level compared to the standard expression level is indicative of a disorder.

[0334] In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

#### **Uses of the Polypeptides**

[0335] Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

[0336] Polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays such as, for example, ABC immunoperoxidase (Hsu et al., J. Histochem. Cytochem. 29:577-580 (1981)) or cell type(s) (e.g., immunocytochemistry assays).

[0337] Antibodies can be used to assay levels of polypeptides encoded by polynucleotides of the invention in a biological sample using classical immunohistological methods known to those of skill in the art (see, e.g., Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine ( $^{131}\text{I}$ ,  $^{125}\text{I}$ ,  $^{123}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{115\text{m}}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{112}\text{In}$ ,  $^{111}\text{In}$ ), and technetium ( $^{99}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ), thallium ( $^{201}\text{Tl}$ ), gallium ( $^{68}\text{Ga}$ ,  $^{67}\text{Ga}$ ), palladium ( $^{103}\text{Pd}$ ), molybdenum ( $^{99}\text{Mo}$ ), xenon ( $^{133}\text{Xe}$ ), fluorine ( $^{18}\text{F}$ ),  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ ,  $^{159}\text{Gd}$ ,  $^{149}\text{Pm}$ ,  $^{140}\text{La}$ ,  $^{175}\text{Yb}$ ,  $^{166}\text{Ho}$ ,  $^{90}\text{Y}$ ,  $^{47}\text{Sc}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{142}\text{Pr}$ ,  $^{105}\text{Rh}$ ,  $^{97}\text{Ru}$ ; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0338] In addition to assaying levels of polypeptide of the present invention in a biological sample, proteins can also be detected *in vivo* by imaging. Antibody labels or markers for *in vivo* imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

[0339] An ovarian antigen-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example,  $^{131}\text{I}$ ,  $^{112}\text{In}$ ,  $^{99\text{m}}\text{Tc}$ , ( $^{131}\text{I}$ ,  $^{125}\text{I}$ ,  $^{123}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{115\text{m}}\text{In}$ ,  $^{113\text{m}}\text{In}$ ,  $^{112}\text{In}$ ,  $^{111}\text{In}$ ), and technetium ( $^{99}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ), thallium ( $^{201}\text{Tl}$ ), gallium ( $^{68}\text{Ga}$ ,  $^{67}\text{Ga}$ ), palladium ( $^{103}\text{Pd}$ ), molybdenum ( $^{99}\text{Mo}$ ), xenon ( $^{133}\text{Xe}$ ), fluorine ( $^{18}\text{F}$ ,  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ ,  $^{159}\text{Gd}$ ,  $^{149}\text{Pm}$ ,  $^{140}\text{La}$ ,  $^{175}\text{Yb}$ ,  $^{166}\text{Ho}$ ,  $^{90}\text{Y}$ ,  $^{47}\text{Sc}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{142}\text{Pr}$ ,  $^{105}\text{Rh}$ ,  $^{97}\text{Ru}$ ), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for ovarian disorders. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety



needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of  $^{99m}\text{Tc}$ . The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which express the polypeptide encoded by a polynucleotide of the invention. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in *Tumor Imaging: The Radiochemical Detection of Cancer*, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

[0340] In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

[0341] In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

[0342] In a preferred embodiment, the invention provides a method for the specific destruction of ovarian and/or breast cells (e.g., aberrant ovarian and/or breast cells, ovarian and/or breast neoplasm) by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) in association with toxins or cytotoxic prodrugs. In another preferred embodiment the invention provides a method for the specific destruction of tissues/cells corresponding to the library source relating to a polynucleotide sequence of the invention as disclosed in column 7 of Table 1 by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

[0343] By "toxin" is meant one or more compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins,

catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example,  $^{213}\text{Bi}$ , or other radioisotopes such as, for example,  $^{103}\text{Pd}$ ,  $^{133}\text{Xe}$ ,  $^{131}\text{I}$ ,  $^{111}\text{In}$ ,  $^{68}\text{Ge}$ ,  $^{57}\text{Co}$ ,  $^{65}\text{Zn}$ ,  $^{85}\text{Sr}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{90}\text{Y}$ ,  $^{153}\text{Sm}$ ,  $^{153}\text{Gd}$ ,  $^{169}\text{Yb}$ ,  $^{51}\text{Cr}$ ,  $^{54}\text{Mn}$ ,  $^{75}\text{Se}$ ,  $^{113}\text{Sn}$ ,  $^{90}\text{Yttrium}$ ,  $^{117}\text{Tin}$ ,  $^{186}\text{Rhenium}$ ,  $^{166}\text{Holmium}$ , and  $^{188}\text{Rhenium}$ ; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0344] In a specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope  $^{90}\text{Y}$ . In another specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope  $^{111}\text{In}$ . In a further specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope  $^{131}\text{I}$ .

[0345] Techniques known in the art may be applied to label polypeptides of the invention (including antibodies). Such techniques include, but are not limited to, the use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361; 5,505,931; 5,489,425; 5,435,990; 5,428,139; 5,342,604; 5,274,119; 4,994,560; and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety).

[0346] Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression level of a polypeptide of the present invention in cells or body fluid of an individual; and (b) comparing the assayed polypeptide expression level

with a standard polypeptide expression level, whereby an increase or decrease in the assayed polypeptide expression level compared to the standard expression level is indicative of a disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

[0347] Moreover, polypeptides of the present invention can be used to treat or prevent diseases or conditions of the ovaries and/or breast such as, for example, neoplastic disorders (e.g., ovarian Krukenberg tumor, malignant mixed Mullerian tumors, and/or as described under "Hyperproliferative Disorders" below), infectious diseases (e.g., mastitis, oophoritis, and/or as described under "Infectious Diseases" below), and inflammatory diseases (e.g., abscesses and/or as described under "Immune Disorders" below), and as described under "Reproductive System Disorders" below. In preferred embodiments, polynucleotides expressed in a particular tissue type (see, e.g., Table 1, column 7) are used to diagnose, detect, prevent, treat and/or prognose disorders associated with the tissue type. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the activity of a polypeptide (e.g., an oncogene or tumor suppressor), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

[0348] Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease (as described *supra*, and elsewhere herein). For example, administration of an antibody directed to a polypeptide of the present invention can bind, and/or neutralize the polypeptide, and/or reduce overproduction of the polypeptide.

Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

[0349] At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the biological activities described herein.

### **Diagnostic Assays**

[0350] The compounds of the present invention are useful for diagnosis, treatment, prevention and/or prognosis of various ovary related disorders in mammals, preferably humans. Such disorders include, but are not limited to, neoplastic disorders (e.g., ovarian Krukenberg tumor, malignant mixed Mullerian tumors, and/or as described under "Hyperproliferative Disorders" below), infectious diseases (e.g., mastitis, oophoritis, and/or as described under "Infectious Diseases" below), and inflammatory diseases (e.g., abscesses and/or as described under "Immune Disorders" below), and as described under "Reproductive System Disorders" below. In preferred embodiments, polynucleotides expressed in a particular tissue type (see, e.g., Table 1, column 7) are used to diagnose, detect, prevent, treat and/or prognose disorders associated with the tissue type.

[0351] Ovarian antigens are expressed in reproductive tissues, with an increased expression level in the ovaries. For a number of ovarian -related disorders, substantially altered (increased or decreased) levels of ovarian antigen gene expression can be detected in ovarian tissue or other cells or bodily fluids (e.g., sera, plasma, urine, semen, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" ovarian antigen gene expression level, that is, the ovarian antigen expression level in ovarian tissues or bodily fluids from an individual not having the ovarian disorder. Thus, the invention provides a diagnostic method useful during diagnosis of an ovarian disorder, which involves measuring the expression level of the gene encoding the ovarian associated polypeptide in ovarian tissue or other cells or body fluid from an individual and comparing the measured gene expression level with a standard ovarian antigens gene

expression level, whereby an increase or decrease in the gene expression level(s) compared to the standard is indicative of an ovarian disorder.

[0352] In specific embodiments, the invention provides a diagnostic method useful during diagnosis of a disorder of a normal or diseased tissue/cell source corresponding to column 7 of Table 1, which involves measuring the expression level of the coding sequence of a polynucleotide sequence associated with this tissue/cell source as disclosed in Table 1 in the tissue/cell source or other cells or body fluid from an individual and comparing the expression level of the coding sequence with a standard expression level of the coding sequence of a polynucleotide sequence, whereby an increase or decrease in the gene expression level(s) compared to the standard is indicative of a disorder of a normal or diseased tissue/cell source corresponding to column 7 of Table 1.

[0353] In particular, it is believed that certain tissues in mammals with cancer of cells or tissue of the ovaries and/or breast express significantly enhanced or reduced levels of normal or altered ovarian antigen expression and mRNA encoding the ovarian associated polypeptide when compared to a corresponding "standard" level. Further, it is believed that enhanced or depressed levels of the ovarian associated polypeptide can be detected in certain body fluids (e.g., sera, plasma, urine, and spinal fluid) or cells or tissue from mammals with such a cancer when compared to sera from mammals of the same species not having the cancer.

[0354] For example, as disclosed herein, ovarian associated polypeptides of the invention are expressed in the ovaries. Accordingly, polynucleotides of the invention (e.g., polynucleotide sequences complementary to all or a portion of an ovarian antigen mRNA nucleotide sequence of SEQ ID NO:X, nucleotide sequence encoding SEQ ID NO:Y, nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:X and/or a nucleotide sequence delineated by columns 8 and 9 of Table 2) and antibodies (and antibody fragments) directed against the polypeptides of the invention may be used to quantitate or qualitate concentrations of cells of the ovaries expressing ovarian antigens, preferably on their cell surfaces. These polynucleotides and antibodies additionally have diagnostic applications in detecting abnormalities in the level of ovarian antigens gene expression, or abnormalities in the structure and/or temporal, tissue, cellular, or subcellular location of ovarian antigens. These diagnostic assays may be performed in

*vivo* or *in vitro*, such as, for example, on blood samples, biopsy tissue or autopsy tissue. In specific embodiments, polynucleotides and antibodies of the invention are used to quantitate or qualitate tissues/cells corresponding to the library source disclosed in column 7 of Table 1 expressing the corresponding ovarian sequence disclosed in the same row of Table 1, preferably on their cell surface.

[0355] Thus, the invention provides a diagnostic method useful during diagnosis of an ovarian disorder, including cancers, which involves measuring the expression level of the gene encoding the ovarian antigen polypeptide in ovarian tissue or other cells or body fluid from an individual and comparing the measured gene expression level with a standard ovarian antigen gene expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of an ovarian disorder. In specific embodiments, polynucleotides and antibodies of the invention are used to quantitate or qualitate tissues/cells corresponding to the library source disclosed in column 7 of Table 1 expressing the corresponding ovarian sequence disclosed in the same row of Table 1, preferably on their cell surface.

[0356] Where a diagnosis of a disorder in the ovaries including diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed ovarian antigen gene expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

[0357] By "assaying the expression level of the gene encoding the ovarian associated polypeptide" is intended qualitatively or quantitatively measuring or estimating the level of the ovarian antigen polypeptide or the level of the mRNA encoding the ovarian antigen polypeptide in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the ovarian associated polypeptide level or mRNA level in a second biological sample). Preferably, the ovarian antigen polypeptide expression level or mRNA level in the first biological sample is measured or estimated and compared to a standard ovarian antigen polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the disorder or being determined by averaging levels from a population of individuals not having a disorder of

the ovaries. As will be appreciated in the art, once a standard ovarian antigen polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

[0358] By "biological sample" is intended any biological sample obtained from an individual, cell line, tissue culture, or other source containing ovarian antigen polypeptides (including portions thereof) or mRNA. As indicated, biological samples include body fluids (such as sera, plasma, urine, synovial fluid and spinal fluid) which contain cells expressing ovarian antigen polypeptides, ovarian tissue, and other tissue sources found to express the full length or fragments thereof of a ovarian antigen. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

[0359] Total cellular RNA can be isolated from a biological sample using any suitable technique such as the single-step guanidinium-thiocyanate-phenol-chloroform method described in Chomczynski and Sacchi, *Anal. Biochem.* 162:156-159 (1987). Levels of mRNA encoding the ovarian antigen polypeptides are then assayed using any appropriate method. These include Northern blot analysis, S1 nuclease mapping, the polymerase chain reaction (PCR), reverse transcription in combination with the polymerase chain reaction (RT-PCR), and reverse transcription in combination with the ligase chain reaction (RT-LCR).

[0360] The present invention also relates to diagnostic assays such as quantitative and diagnostic assays for detecting levels of ovarian antigen polypeptides, in a biological sample (e.g., cells and tissues), including determination of normal and abnormal levels of polypeptides. Thus, for instance, a diagnostic assay in accordance with the invention for detecting over-expression of ovarian antigens compared to normal control tissue samples may be used to detect the presence of tumors. Assay techniques that can be used to determine levels of a polypeptide, such as an ovarian antigen polypeptide of the present invention in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radioimmunoassays, competitive-binding assays, Western Blot analysis and ELISA assays. Assaying ovarian antigen polypeptide levels in a biological sample can occur using any art-known method.

[0361] Assaying ovarian antigen polypeptide levels in a biological sample can occur using antibody-based techniques. For example, ovarian antigen polypeptide

expression in tissues can be studied with classical immunohistological methods (Jalkanen et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting ovarian antigen polypeptide gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine ( $^{125}\text{I}$ ,  $^{121}\text{I}$ ), carbon ( $^{14}\text{C}$ ), sulfur ( $^{35}\text{S}$ ), tritium ( $^3\text{H}$ ), indium ( $^{112}\text{In}$ ), and technetium ( $^{99\text{m}}\text{Tc}$ ), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0362] The tissue or cell type to be analyzed will generally include those which are known, or suspected, to express the ovarian antigen gene (such as, for example, cells of the ovaries and/or breast or ovarian and/or breast cancer). The protein isolation methods employed herein may, for example, be such as those described in Harlow and Lane (Harlow, E. and Lane, D., 1988, "Antibodies: A Laboratory Manual", Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York), which is incorporated herein by reference in its entirety. The isolated cells can be derived from cell culture or from a patient. The analysis of cells taken from culture may be a necessary step in the assessment of cells that could be used as part of a cell-based gene therapy technique or, alternatively, to test the effect of compounds on the expression of the ovarian antigen gene.

[0363] For example, antibodies, or fragments of antibodies, such as those described herein, may be used to quantitatively or qualitatively detect the presence of ovarian antigen gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.

[0364] In a preferred embodiment, antibodies, or fragments of antibodies directed to any one or all of the predicted epitope domains of the ovarian antigen polypeptides (Shown in Table 1, column 6) may be used to quantitatively or qualitatively detect the presence of ovarian antigen gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.



[0365] In an additional preferred embodiment, antibodies, or fragments of antibodies directed to a conformational epitope of an ovarian antigen may be used to quantitatively or qualitatively detect the presence of ovarian antigen gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.

[0366] The antibodies (or fragments thereof), and/or ovarian antigen polypeptides of the present invention may, additionally, be employed histologically, as in immunofluorescence, immunoelectron microscopy or non-immunological assays, for in situ detection of ovarian antigen gene products or conserved variants or peptide fragments thereof. In situ detection may be accomplished by removing a histological specimen from a patient, and applying thereto a labeled antibody or ovarian antigen polypeptide of the present invention. The antibody (or fragment thereof) or ovarian antigen polypeptide is preferably applied by overlaying the labeled antibody (or fragment) onto a biological sample. Through the use of such a procedure, it is possible to determine not only the presence of the ovarian antigen gene product, or conserved variants or peptide fragments, or ovarian antigen polypeptide binding, but also its distribution in the examined tissue. Using the present invention, those of ordinary skill will readily perceive that any of a wide variety of histological methods (such as staining procedures) can be modified in order to achieve such in situ detection.

[0367] Immunoassays and non-immunoassays for ovarian antigen gene products or conserved variants or peptide fragments thereof will typically comprise incubating a sample, such as a biological fluid, a tissue extract, freshly harvested cells, or lysates of cells which have been incubated in cell culture, in the presence of a detectably labeled antibody capable of binding ovarian antigen gene products or conserved variants or peptide fragments thereof, and detecting the bound antibody by any of a number of techniques well-known in the art.

[0368] The biological sample may be brought in contact with and immobilized onto a solid phase support or carrier such as nitrocellulose, or other solid support which is capable of immobilizing cells, cell particles or soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled anti-

ovarian antigen antibody or detectable ovarian antigen polypeptide. The solid phase support may then be washed with the buffer a second time to remove unbound antibody or polypeptide. Optionally the antibody is subsequently labeled. The amount of bound label on solid support may then be detected by conventional means.

[0369] By "solid phase support or carrier" is intended any support capable of binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention. The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to an antigen or antibody. Thus, the support configuration may be spherical, as in a bead, or cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads. Those skilled in the art will know many other suitable carriers for binding antibody or antigen, or will be able to ascertain the same by use of routine experimentation.

[0370] The binding activity of a given lot of anti-ovarian antigen antibody or ovarian antigen polypeptide may be determined according to well known methods. Those skilled in the art will be able to determine operative and optimal assay conditions for each determination by employing routine experimentation.

[0371] In addition to assaying ovarian antigen polypeptide levels or polynucleotide levels in a biological sample obtained from an individual, ovarian antigen polypeptide or polynucleotide can also be detected *in vivo* by imaging. For example, in one embodiment of the invention, ovarian antigen polypeptide and/or anti- ovarian antigen antibodies are used to image ovarian diseased cells, such as neoplasms. In another embodiment, ovarian antigen polynucleotides of the invention (e.g., polynucleotides complementary to all or a portion of ovarian antigen mRNA) and/or anti- ovarian antigen antibodies (e.g., antibodies directed to any one or a combination of the epitopes of ovarian antigens, antibodies directed to a conformational epitope of ovarian antigens, antibodies directed to the full length polypeptide expressed on the cell surface of a mammalian cell) are used to image diseased or neoplastic cells of the ovaries.

[0372] Antibody labels or markers for *in vivo* imaging of ovarian antigen polypeptides include those detectable by X-radiography, NMR, MRI, CAT-scans or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma. Where *in vivo* imaging is used to detect enhanced levels of ovarian antigen polypeptides for diagnosis in humans, it may be preferable to use human antibodies or "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using techniques described herein or otherwise known in the art. For example methods for producing chimeric antibodies are known in the art. See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).

[0373] Additionally, any ovarian antigen polypeptides whose presence can be detected, can be administered. For example, ovarian antigen polypeptides labeled with a radio-opaque or other appropriate compound can be administered and visualized *in vivo*, as discussed, above for labeled antibodies. Further such ovarian antigen polypeptides can be utilized for *in vitro* diagnostic procedures.

[0374] An ovarian antigen polypeptide-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example,  $^{131}\text{I}$ ,  $^{112}\text{In}$ ,  $^{99\text{m}}\text{Tc}$ ), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for an ovarian and/or breast disorder. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of  $^{99\text{m}}\text{Tc}$ . The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain ovarian antigen protein. *In vivo* tumor imaging is described in S.W.

Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in *Tumor Imaging: The Radiochemical Detection of Cancer*, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

[0375] With respect to antibodies, one of the ways in which the anti- ovarian antigen antibody can be detectably labeled is by linking the same to an enzyme and using the linked product in an enzyme immunoassay (EIA) (Voller, A., "The Enzyme Linked Immunosorbent Assay (ELISA)", 1978, Diagnostic Horizons 2:1-7, Microbiological Associates Quarterly Publication, Walkersville, MD); Voller et al., J. Clin. Pathol. 31:507-520 (1978); Butler, J.E., Meth. Enzymol. 73:482-523 (1981); Maggio, E. (ed.), 1980, Enzyme Immunoassay, CRC Press, Boca Raton, FL.; Ishikawa, E. et al., (eds.), 1981, Enzyme Immunoassay, Kaku Shoin, Tokyo). The enzyme which is bound to the antibody will react with an appropriate substrate, preferably a chromogenic substrate, in such a manner as to produce a chemical moiety which can be detected, for example, by spectrophotometric, fluorimetric or by visual means. Enzymes which can be used to detectably label the antibody include, but are not limited to, malate dehydrogenase, staphylococcal nuclease, delta-5-steroid isomerase, yeast alcohol dehydrogenase, alpha-glycerophosphate dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, beta-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase and acetylcholinesterase. Additionally, the detection can be accomplished by colorimetric methods which employ a chromogenic substrate for the enzyme. Detection may also be accomplished by visual comparison of the extent of enzymatic reaction of a substrate in comparison with similarly prepared standards.

[0376] Detection may also be accomplished using any of a variety of other immunoassays. For example, by radioactively labeling the antibodies or antibody fragments, it is possible to detect ovarian antigens through the use of a radioimmunoassay (RIA) (see, for example, Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, The Endocrine Society, March, 1986, which is incorporated by reference herein). The radioactive isotope can be detected by means including, but not limited to, a gamma counter, a scintillation counter, or autoradiography.

[0377] It is also possible to label the antibody with a fluorescent compound. When the fluorescently labeled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, ophthaldehyde and fluorescamine.

[0378] The antibody can also be detectably labeled using fluorescence emitting metals such as  $^{152}\text{Eu}$ , or others of the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

[0379] The antibody also can be detectably labeled by coupling it to a chemiluminescent compound. The presence of the chemiluminescent-tagged antibody is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of particularly useful chemiluminescent labeling compounds are luminol, isoluminol, therrromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

[0380] Likewise, a bioluminescent compound may be used to label the antibody of the present invention. Bioluminescence is a type of chemiluminescence found in biological systems in, which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

#### **Methods for Detecting Ovarian and/or Breast Disease, Including Cancer**

[0381] In general, an ovarian and/or breast disease or cancer may be detected in a patient based on the presence of one or more ovarian antigen proteins of the invention and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine, and/or tumor biopsies) obtained from the patient. In other words, such proteins and/or polynucleotides may be used as markers to indicate the presence or absence of an ovarian and/or breast disease or disorder, including cancer. Cancers that may be diagnosed, and/or prognosed using the compositions of the invention include but are not limited to, ovarian and/or breast cancer. In addition, such proteins and/or polynucleotidse

may be useful for the detection of other diseases and cancers, including cancers of tissues/cells corresponding to the library source disclosed in column 7 of Table 1 expressing the corresponding ovarian sequence disclosed in the same row of Table 1. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding ovarian antigen polypeptides, which is also indicative of the presence or absence of an ovarian and/or breast disease or disorder, including cancer. In general, ovarian antigen polypeptides should be present at a level that is at least three fold higher in diseased tissue than in normal tissue.

[0382] There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *supra*. In general, the presence or absence of an ovarian and/or breast disease in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

[0383] In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the ovarian antigen polypeptide of the invention from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include ovarian antigen polypeptides and portions thereof, or antibodies, to which the binding agent binds, as described above.

[0384] The solid support may be any material known to those of skill in the art to which ovarian antigen polypeptides of the invention may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for the suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 ug, and preferably about 100 ng to about 1 ug, is sufficient to immobilize an adequate amount of binding agent.

[0385] Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

### **Gene Therapy Methods**

[0386] Also encompassed by the present invention are gene therapy methods for treating or preventing disorders, diseases and conditions. The gene therapy methods relate to the introduction of nucleic acid (DNA, RNA and antisense DNA or RNA) sequences

into an animal to achieve expression of an ovarian antigen of the present invention. This method requires a polynucleotide, which codes for a polypeptide of the present invention operatively linked to a promoter and any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques are known in the art, see, for example, WO90/11092, which is herein incorporated by reference.

[0387] Thus, for example, cells from a patient may be engineered with a polynucleotide (DNA or RNA) comprising a promoter operably linked to a polynucleotide of the present invention *ex vivo*, with the engineered cells then being provided to a patient to be treated with the polypeptide of the present invention. Such methods are well-known in the art. For example, see Belldgrun, A., et al., *J. Natl. Cancer Inst.* 85: 207-216 (1993); Ferrantini, M. et al., *Cancer Research* 53: 1107-1112 (1993); Ferrantini, M. et al., *J. Immunology* 153: 4604-4615 (1994); Kaido, T., et al., *Int. J. Cancer* 60: 221-229 (1995); Ogura, H., et al., *Cancer Research* 50: 5102-5106 (1990); Santodonato, L., et al., *Human Gene Therapy* 7:1-10 (1996); Santodonato, L., et al., *Gene Therapy* 4:1246-1255 (1997); and Zhang, J.-F. et al., *Cancer Gene Therapy* 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the artery, or through catheter injection.

[0388] As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

[0389] In one embodiment, the polynucleotide of the present invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotide of the present invention can also be delivered in liposome formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods



are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

[0390] The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Appropriate vectors include pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1, and pRc/CMV2 available from Invitrogen. Other suitable vectors will be readily apparent to the skilled artisan.

[0391] Any strong promoter known to those skilled in the art can be used for driving the expression of the polynucleotide sequence. Suitable promoters include adenoviral promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible promoters, such as the MMT promoter, the metallothionein promoter; heat shock promoters; the albumin promoter; the ApoAI promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes Simplex thymidine kinase promoter; retroviral LTRs; the b-actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotide of the present invention.

[0392] Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

[0393] The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular, fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the

space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

[0394] For the naked nucleic acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

[0395] The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

[0396] The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

[0397] The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

[0398] In certain embodiments, the polynucleotide constructs are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations.

However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA (1989) 86:6077-6081, which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem. (1990) 265:10189-10192, which is herein incorporated by reference), in functional form.

[0399] Cationic liposomes are readily available. For example, N[1-2,3-dioleoyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO-BRL, Grand Island, N.Y., (see, also, Felgner et al., Proc. Natl Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

[0400] Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., P. Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

[0401] Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphosphatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

[0402] For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the

addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

[0403] The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g., Straubinger et al., *Methods of Immunology* (1983), 101:512-527, which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include  $\text{Ca}^{2+}$ -EDTA chelation (Papahadjopoulos et al., *Biochim. Biophys. Acta* (1975) 394:483; Wilson et al., *Cell* 17:77 (1979); ether injection (Deamer, D. and Bangham, A., *Biochim. Biophys. Acta* 443:629 (1976); Ostro et al., *Biochem. Biophys. Res. Commun.* 76:836 (1977); Fraley et al., *Proc. Natl. Acad. Sci. USA* 76:3348 (1979)); detergent dialysis (Enoch, H. and Strittmatter, P., *Proc. Natl. Acad. Sci. USA* 76:145 (1979)); and reverse-phase evaporation (REV) (Fraley et al., *J. Biol. Chem.* 255:10431 (1980); Szoka et al., *Proc. Natl. Acad. Sci.*

USA 75:145 (1978); Schaefer-Ridder et al., Science 215:166 (1982)), which are herein incorporated by reference.

[0404] Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.

[0405] U.S. Patent No. 5,676,954 (which is herein incorporated by reference) reports on the injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and International Publication No. WO 94/9469 provide methods for delivering DNA-cationic lipid complexes to mammals.

[0406] In certain embodiments, cells are engineered, *ex vivo* or *in vivo*, using a retroviral particle containing RNA which comprises a sequence encoding a polypeptide of the present invention. Retroviruses from which the retroviral plasmid vectors may be derived include, but are not limited to, Moloney Murine-Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

[0407] The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, Human Gene Therapy 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and CaPO<sub>4</sub> precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

[0408] The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding a polypeptide of the present invention. Such retroviral

vector particles then may be employed, to transduce eukaryotic cells, either *in vitro* or *in vivo*. The transduced eukaryotic cells will express a polypeptide of the present invention.

[0409] In certain other embodiments, cells are engineered, *ex vivo* or *in vivo*, with polynucleotide contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses a polypeptide of the present invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have been used as live enteric vaccines for many years with an excellent safety profile (Schwartz, et al., *Am. Rev. Respir. Dis.* 109:233-238 (1974)). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld et al., *Science* 252:431-434 (1991); Rosenfeld et al., *Cell* 68:143-155 (1991)). Furthermore, extensive studies to attempt to establish adenovirus as a causative agent in human cancer were uniformly negative (Green et al., *Proc. Natl. Acad. Sci. USA* 76:6606 (1979)).

[0410] Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, *Curr. Opin. Genet. Devel.* 3:499-503 (1993); Rosenfeld et al., *Cell* 68:143-155 (1992); Engelhardt et al., *Human Genet. Ther.* 4:759-769 (1993); Yang et al., *Nature Genet.* 7:362-369 (1994); Wilson et al., *Nature* 365:691-692 (1993); and U.S. Patent No. 5,652,224, which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express Ela and Elb, which complement the defective adenoviruses by providing the products of the genes deleted from the vector. In addition to Ad2, other varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

[0411] Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in

one or more of all or a portion of the following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

[0412] In certain other embodiments, the cells are engineered, *ex vivo* or *in vivo*, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper viruses to produce infectious particles (Muzyczka, N., Curr. Topics in Microbiol. Immunol. 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

[0413] For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate-precipitation, etc. Appropriate helper viruses include adenoviruses, cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct. These viral particles are then used to transduce eukaryotic cells, either *ex vivo* or *in vivo*. The transduced cells will contain the polynucleotide construct integrated into its genome, and will express a polypeptide of the invention.

[0414] Another method of gene therapy involves operably associating heterologous control regions and endogenous ovarian antigen polynucleotide sequences (e.g., encoding an ovarian antigen polypeptide of the present invention) via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), which are herein

incorporated by reference. This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

[0415] Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5' end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

[0416] The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

[0417] The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

[0418] The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

[0419] The polynucleotide encoding a polypeptide of the present invention may contain a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide to be expressed



towards or at the 5' end of the coding region. The signal sequence may be homologous or heterologous to the ovarian antigen polynucleotide of interest and may be homologous or heterologous to the cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

[0420] Any mode of administration of any of the above-described polynucleotides constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., "gene guns"), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral or suppository solid (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers (Kaneda et al., Science 243:375 (1989)).

[0421] A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting the composition centimeters and preferably, millimeters within arteries.

[0422] Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue inside the wound.

[0423] Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a particular site. In specific embodiments, suitable delivery vehicles for use with systemic administration comprise liposomes comprising polypeptides of the invention for targeting the vehicle to a particular site.

[0424] Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad. Sci. USA 189:11277-11281, 1992, which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

[0425] Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise condition requiring treatment and its severity, and the route of administration. The frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian.

[0426] Therapeutic compositions of the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits sheep, cattle, horses and pigs, with humans being particularly preferred.

### **Biological Activities**

[0427] Polynucleotides or polypeptides, or agonists or antagonists of the present invention, can be used in assays to test for one or more biological activities. If these polynucleotides or polypeptides, or agonists or antagonists of the present invention, do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides, and agonists or antagonists could be used to treat, prevent diagnose and/or prognose the associated disease.

[0428] The ovarian antigen polynucleotides and polypeptides of the invention are predicted to have predominant expression in ovarian tissues.

[0429] Thus, the ovarian antigens of the invention may be useful as therapeutic molecules. Each would be useful for diagnosis, detection, treatment and/or prevention of diseases or disorders of the ovaries and/or breast, neoplastic disorders (e.g., ovarian Krukenberg tumor, malignant mixed Mullerian tumors, and/or as described under "Hyperproliferative Disorders" below), infectious diseases (e.g., mastitis, oophoritis, and/or as described under "Infectious Diseases" below), and inflammatory diseases (e.g., abscesses and/or as described under "Immune Disorders" below), and as described under "Reproductive System Disorders" below.

[0430] In a preferred embodiment, polynucleotides of the invention (e.g., a nucleic acid sequence of SEQ ID NO:X or the complement thereof; or the cDNA sequence contained in Clone ID NO:Z, or fragments or variants thereof) and/or polypeptides of the invention (e.g., an amino acid sequence contained in SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, or the complement thereof, an amino acid sequence encoded by the cDNA sequence contained in Clone ID NO:Z and fragments or variants thereof as described herein) are useful for the diagnosis, detection, treatment, and/or prevention of diseases or disorders of the tissues/cells corresponding to the library source disclosed in column 7 of Table 1 expressing the corresponding ovarian sequence disclosed in the same row of Table 1. In certain embodiments, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to diagnose and/or prognose diseases and/or disorders associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1, column 7 (Tissue Distribution Library Code).

[0431] Particularly, the ovarian antigens may be a useful therapeutic for ovarian and/or breast cancer. Treatment, diagnosis, detection, and/or prevention of ovarian and/or breast disorders could be carried out using an ovarian antigen or soluble form of an ovarian antigen, an ovarian antigen ligand, gene therapy, or ex vivo applications. Moreover, inhibitors of an ovarian antigen, either blocking antibodies or mutant forms, could modulate the expression of the ovarian antigen. These inhibitors may be useful to

treat, diagnose, detect, and/or prevent diseases associated with the misregulation of an ovarian antigen.

[0432] In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells (e.g., normal or diseased ovarian and/or breast cells) by administering polypeptides of the invention (e.g., ovarian antigen polypeptides or anti- ovarian antigen antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell (e.g., an aberrant ovarian and/or breast cell or ovarian and/or breast cancer cell). In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

[0433] In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of aberrant ovarian and/or breast cells, including, but not limited to, ovarian and/or breast tumor cells) by administering polypeptides of the invention (e.g., ovarian antigen polypeptides or fragments thereof, or anti- ovarian antigen antibodies) in association with toxins or cytotoxic prodrugs.

[0434] By "toxin" is meant compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, cytotoxins (cytotoxic agents), or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example,  $^{213}\text{Bi}$ , or other radioisotopes such as, for example,  $^{103}\text{Pd}$ ,  $^{133}\text{Xe}$ ,  $^{131}\text{I}$ ,  $^{68}\text{Ge}$ ,  $^{57}\text{Co}$ ,  $^{65}\text{Zn}$ ,  $^{85}\text{Sr}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{90}\text{Y}$ ,  $^{153}\text{Sm}$ ,  $^{153}\text{Gd}$ ,  $^{169}\text{Yb}$ ,  $^{51}\text{Cr}$ ,  $^{54}\text{Mn}$ ,  $^{75}\text{Se}$ ,  $^{113}\text{Sn}$ ,

<sup>90</sup>Yttrium, <sup>117</sup>Tin, <sup>186</sup>Rhenium, <sup>166</sup>Holmium, and <sup>188</sup>Rhenium; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0435] Techniques known in the art may be applied to label antibodies of the invention. Such techniques include, but are not limited to, the use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361; 5,505,931; 5,489,425; 5,435,990; 5,428,139; 5,342,604; 5,274,119; 4,994,560; and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety). A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis- dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

[0436] By "cytotoxic prodrug" is meant a non-toxic compound that is converted by an enzyme, normally present in the cell, into a cytotoxic compound. Cytotoxic prodrugs that may be used according to the methods of the invention include, but are not limited to, glutamyl derivatives of benzoic acid mustard alkylating agent, phosphate derivatives of etoposide or mitomycin C, cytosine arabinoside, daunorubisin, and phenoxyacetamide derivatives of doxorubicin.

[0437] It will be appreciated that conditions caused by a decrease in the standard or normal level of an ovarian antigen activity in an individual, particularly disorders of the ovaries and/or breast, can be treated by administration of an ovarian antigen polypeptide (e.g., such as, for example, the complete ovarian antigen polypeptide, the soluble form of

the extracellular domain of an ovarian antigen polypeptide, or cells expressing the complete protein) or agonist. Thus, the invention also provides a method of treatment of an individual in need of an increased level of ovarian antigen activity comprising administering to such an individual a pharmaceutical composition comprising an amount of an isolated ovarian antigen polypeptide of the invention, or agonist thereof (e.g., an agonistic anti-ovarian antigen antibody), effective to increase the ovarian antigen activity level in such an individual.

[0438] It will also be appreciated that conditions caused by a increase in the standard or normal level of ovarian antigen activity in an individual, particularly disorders of the ovaries and/or breast, can be treated by administration of ovarian antigen polypeptides (e.g., such as, for example, the complete ovarian antigen polypeptide, the soluble form of the extracellular domain of an ovarian antigen polypeptide, or cells expressing the complete protein) or antagonist (e.g., an antagonistic ovarian antigen antibody). Thus, the invention also provides a method of treatment of an individual in need of an decreased level of ovarian antigen activity comprising administering to such an individual a pharmaceutical composition comprising an amount of an isolated ovarian antigen polypeptide of the invention, or antagonist thereof (e.g., an antagonistic anti-ovarian antigen antibody), effective to decrease the ovarian antigen activity level in such an individual.

[0439] More generally, polynucleotides, translation products and antibodies corresponding to this gene may be useful for the diagnosis, prognosis, prevention, and/or treatment of diseases and/or disorders associated with the following systems.

#### **Reproductive System Disorders**

[0440] The polynucleotides or polypeptides, or agonists or antagonists of the invention may be used for the diagnosis, treatment, or prevention of diseases and/or disorders of the reproductive system. Reproductive system disorders that can be treated by the compositions of the invention, include, but are not limited to, reproductive system injuries, infections, neoplastic disorders, congenital defects, and diseases or disorders which result in infertility, complications with pregnancy, labor, or parturition, and postpartum difficulties.

[0441] Reproductive system disorders and/or diseases include diseases and/or disorders of the testes, including, but not limited to, testicular atrophy, testicular feminization, cryptorchism (unilateral and bilateral), anorchia, ectopic testis, epididymitis and orchitis (typically resulting from infections such as, for example, gonorrhea, mumps, tuberculosis, and syphilis), testicular torsion, vasitis nodosa, germ cell tumors (e.g., seminomas, embryonal cell carcinomas, teratocarcinomas, choriocarcinomas, yolk sac tumors, and teratomas), stromal tumors (e.g., Leydig cell tumors), hydrocele, hematocele, varicocele, spermatocele, inguinal hernia, and disorders of sperm production (e.g., immotile cilia syndrome, aspermia, asthenozoospermia, azoospermia, oligospermia, and teratozoospermia).

[0442] Reproductive system disorders also include, but are not limited to, disorders of the prostate gland, such as acute non-bacterial prostatitis, chronic non-bacterial prostatitis, acute bacterial prostatitis, chronic bacterial prostatitis, prostatodynia, prostatosis, granulomatous prostatitis, malacoplakia, benign prostatic hypertrophy or hyperplasia, and prostate neoplastic disorders, including adenocarcinomas, transitional cell carcinomas, ductal carcinomas, and squamous cell carcinomas.

[0443] Additionally, the compositions of the invention may be useful in the diagnosis, treatment, and/or prevention of disorders or diseases of the penis and urethra, including, but not limited to, inflammatory disorders, such as balanoposthitis, balanitis xerotica obliterans, phimosis, paraphimosis, syphilis, herpes simplex virus, gonorrhea, non-gonococcal urethritis, chlamydia, mycoplasma, trichomonas, HIV, AIDS, Reiter's syndrome, condyloma acuminatum, condyloma latum, and pearly penile papules; urethral abnormalities, such as hypospadias, epispadias, and phimosis; premalignant lesions, including Erythroplasia of Queyrat, Bowen's disease, Bowenoid papulosis, giant condyloma of Buscke-Lowenstein, and verrucous carcinoma; penile cancers, including squamous cell carcinomas, carcinoma in situ, verrucous carcinoma, and disseminated penile carcinoma; urethral neoplastic disorders, including penile urethral carcinoma, bulbomembranous urethral carcinoma, and prostatic urethral carcinoma; and erectile disorders, such as priapism, Peyronie's disease, erectile dysfunction, and impotence.

[0444] Moreover, diseases and/or disorders of the vas deferens include, but are not limited to, vasculitis and CBAVD (congenital bilateral absence of the vas deferens);

additionally, the polynucleotides, polypeptides, agonists or antagonists of the present invention may be used in the diagnosis and/or prevention of diseases and/or disorders of the seminal vesicles, including, but not limited to, hydatid disease, congenital chloride diarrhea, and polycystic kidney.

[0445] Other disorders and/or conditions of the male reproductive system that may be diagnosed, treated, and/or prevented by the invention include, but are not limited to, Klinefelter's syndrome, premature ejaculation, diabetes mellitus, cystic fibrosis, Klinefelter's syndrome, high fever, multiple sclerosis, and gynecomastia.

[0446] Further, the polynucleotides, agonists, and antagonists of the present invention may be used in the diagnosis, treatment, and/or prevention of diseases and/or disorders of the vagina including, but not limited to, bacterial vaginosis, candida vaginitis, herpes simplex chancroid, granuloma inguinale, lymphogranuloma venereum, scabies, human immunodeficiency virus, vaginal trauma, vulvar trauma, adenosis, chlamydia vaginitis, trichomonas vaginitis, condyloma acuminatum, syphilis, molluscum contagiosum, vaginitis, Paget's disease, lichen sclerosus, lichen planus, vulvodynia, vaginismus, vulvovaginitis, vulvar vestibulitis, and neoplastic disorders such as squamous cell hyperplasia, clear cell carcinoma, basal cell carcinoma, melanoma of Bartholin's gland, and vulvar intraepithelial neoplasia.

[0447] Disorders and/or diseases that may be diagnosed, treated, and/or prevented with the composition of the invention include, but are not limited to, dysmenorrhea, retroverted uterus, endometriosis, adenomyosis, anovulatory bleeding, amenorrhea, Cushing's syndrome, Asherman's syndrome, premature menopause, precocious puberty, dysfunctional uterine bleeding (e.g., due to aberrant hormonal secretion), neoplastic disorders, such as adenocarcinomas, leiomyosarcomas, and so forth. Additionally, the polypeptides, polynucleotides, or agonists or antagonists of the present invention may be useful as a marker or detector of, as well as in the diagnosis and/or prevention of congenital uterine abnormalities, such as bicornuate uterus, simple unicornuate uterus, unicornuate uterus with a noncavitary endometrium, and unicornuate uterus with a non-



communicating cavitory rudimentary horn, unicornuate uterus with a communicating cavitory horn, arcuate uterus, uterine didelphys, and T-shaped uterus.

[0448] Ovarian diseases and/or disorders that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, anovulation, polycystic ovary syndrome (Stein-Leventhal syndrome), ovarian cysts, ovarian hypofunction, ovarian insensitivity to gonadotropins, ovarian overproduction of androgens, right ovarian vein syndrome, amenorrhea, hirsutism, and ovarian cancer (including, but not limited to, primary and secondary cancerous growth, Sertoli-Leydig tumors, endometrioid carcinoma of the ovary, ovarian papillary serous adenocarcinoma, ovarian mucinous adenocarcinoma, and Ovarian Krukenberg tumors).

[0449] Cervical diseases and/or disorders that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, cervicitis, chronic cervicitis, mucopurulent cervicitis, cervical dysplasia, cervical polyps, Nabothian cysts, cervical erosion, cervical incompetence, and cervical neoplasms (including, for example, cervical carcinoma, squamous metaplasia, squamous cell carcinoma, adenosquamous cell neoplasia, and columnar cell neoplasia).

[0450] Additionally, diseases and/or disorders of the reproductive system that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, disorders and/or diseases of pregnancy, including miscarriage and stillbirth, such as early abortion, late abortion, spontaneous abortion, induced abortion, therapeutic abortion, threatened abortion, missed abortion, incomplete abortion, complete abortion, habitual abortion, missed abortion, and septic abortion; ectopic pregnancy, anemia, Rh incompatibility, vaginal bleeding during pregnancy, gestational diabetes, intrauterine growth retardation, polyhydramnios, HELLP syndrome, abruptio placentae, placenta previa, hyperemesis, preeclampsia, eclampsia, herpes gestationis, and urticaria of pregnancy. Additionally, the polynucleotides, polypeptides, and agonists or antagonists of the present invention may be used in the diagnosis, treatment, and/or prevention of diseases that can complicate pregnancy, including heart disease, heart failure, rheumatic heart disease, congenital heart disease, mitral valve prolapse, high blood pressure, anemia, kidney disease, infectious disease (e.g., rubella, cytomegalovirus, toxoplasmosis, infectious hepatitis, chlamydia, HIV, AIDS, and genital herpes), diabetes mellitus,

Graves' disease, thyroiditis, hypothyroidism, Hashimoto's thyroiditis, chronic active hepatitis, cirrhosis of the liver, primary biliary cirrhosis, asthma, systemic lupus erythematosus, rheumatoid arthritis, myasthenia gravis, idiopathic thrombocytopenic purpura, appendicitis, ovarian cysts, gallbladder disorders, and obstruction of the intestine.

[0451] Complications associated with labor and parturition that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, premature rupture of the membranes, pre-term labor, post-term pregnancy, postmaturity, labor that progresses too slowly, fetal distress (e.g., abnormal heart rate (fetal or maternal), breathing problems, and abnormal fetal position), shoulder dystocia, prolapsed umbilical cord, amniotic fluid embolism, and aberrant uterine bleeding.

[0452] Further, diseases and/or disorders of the postdelivery period, that may be diagnosed, treated, and/or prevented with the compositions of the invention, include, but are not limited to, endometritis, myometritis, parametritis, peritonitis, pelvic thrombophlebitis, pulmonary embolism, endotoxemia, pyelonephritis, saphenous thrombophlebitis, mastitis, cystitis, postpartum hemorrhage, and inverted uterus.

[0453] Other disorders and/or diseases of the female reproductive system that may be diagnosed, treated, and/or prevented by the polynucleotides, polypeptides, and agonists or antagonists of the present invention include, but are not limited to, Turner's syndrome, pseudohermaphroditism, premenstrual syndrome, pelvic inflammatory disease, pelvic congestion (vascular engorgement), frigidity, anorgasmia, dyspareunia, ruptured fallopian tube, and Mittelschmerz.

### **Immune Activity**

[0454] Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, diagnosing and/or prognosing diseases, disorders, and/or conditions of the immune system, by, for example, activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune diseases, disorders, and/or conditions may be genetic, somatic, such as cancer and some

autoimmune diseases, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

[0455] In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to treat diseases and disorders of the immune system and/or to inhibit or enhance an immune response generated by cells associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1, column 7 (Tissue Distribution Library Code).

[0456] Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, diagnosing, and/or prognosing immunodeficiencies, including both congenital and acquired immunodeficiencies. Examples of B cell immunodeficiencies in which immunoglobulin levels B cell function and/or B cell numbers are decreased include: X-linked agammaglobulinemia (Bruton's disease), X-linked infantile agammaglobulinemia, X-linked immunodeficiency with hyper IgM, non X-linked immunodeficiency with hyper IgM, X-linked lymphoproliferative syndrome (XLP), agammaglobulinemia including congenital and acquired agammaglobulinemia, adult onset agammaglobulinemia, late-onset agammaglobulinemia, dysgammaglobulinemia, hypogammaglobulinemia, unspecified hypogammaglobulinemia, recessive agammaglobulinemia (Swiss type), Selective IgM deficiency, selective IgA deficiency, selective IgG subclass deficiencies, IgG subclass deficiency (with or without IgA deficiency), Ig deficiency with increased IgM, IgG and IgA deficiency with increased IgM, antibody deficiency with normal or elevated Igs, Ig heavy chain deletions, kappa chain deficiency, B cell lymphoproliferative disorder (BLPD), common variable immunodeficiency (CVID), common variable immunodeficiency (CVI) (acquired), and transient hypogammaglobulinemia of infancy.

[0457] In specific embodiments, ataxia-telangiectasia or conditions associated with ataxia-telangiectasia are treated, prevented, diagnosed, and/or prognosing using the polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof.

[0458] Examples of congenital immunodeficiencies in which T cell and/or B cell function and/or number is decreased include, but are not limited to: DiGeorge anomaly, severe combined immunodeficiencies (SCID) (including, but not limited to, X-linked SCID, autosomal recessive SCID, adenosine deaminase deficiency, purine nucleoside phosphorylase (PNP) deficiency, Class II MHC deficiency (Bare lymphocyte syndrome), Wiskott-Aldrich syndrome, and ataxia telangiectasia), thymic hypoplasia, third and fourth pharyngeal pouch syndrome, 22q11.2 deletion, chronic mucocutaneous candidiasis, natural killer cell deficiency (NK), idiopathic CD4+ T-lymphocytopenia, immunodeficiency with predominant T cell defect (unspecified), and unspecified immunodeficiency of cell mediated immunity.

[0459] In specific embodiments, DiGeorge anomaly or conditions associated with DiGeorge anomaly are treated, prevented, diagnosed, and/or prognosed using polypeptides or polynucleotides of the invention, or antagonists or agonists thereof.

[0460] Other immunodeficiencies that may be treated, prevented, diagnosed, and/or prognosed using polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof, include, but are not limited to, chronic granulomatous disease, Chédiak-Higashi syndrome, myeloperoxidase deficiency, leukocyte glucose-6-phosphate dehydrogenase deficiency, X-linked lymphoproliferative syndrome (XLP), leukocyte adhesion deficiency, complement component deficiencies (including C1, C2, C3, C4, C5, C6, C7, C8 and/or C9 deficiencies), reticular dysgenesis, thymic aplasia-aplasia, immunodeficiency with thymoma, severe congenital leukopenia, dysplasia with immunodeficiency, neonatal neutropenia, short limbed dwarfism, and Nezelof syndrome-combined immunodeficiency with Igs.

[0461] In a preferred embodiment, the immunodeficiencies and/or conditions associated with the immunodeficiencies recited above are treated, prevented, diagnosed and/or prognosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

[0462] In a preferred embodiment polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used as an agent to boost immunoresponsiveness among immunodeficient individuals. In specific embodiments, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present

invention could be used as an agent to boost immunoresponsiveness among B cell and/or T cell immunodeficient individuals.

[0463] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, diagnosing and/or prognosing autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of polynucleotides and polypeptides of the invention that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

[0464] Autoimmune diseases or disorders that may be treated, prevented, diagnosed and/or prognosed by polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include, but are not limited to, one or more of the following: systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, multiple sclerosis, autoimmune thyroiditis, Hashimoto's thyroiditis, autoimmune hemolytic anemia, hemolytic anemia, thrombocytopenia, autoimmune thrombocytopenia purpura, autoimmune neonatal thrombocytopenia, idiopathic thrombocytopenia purpura, purpura (e.g., Henloch-Scoenlein purpura), autoimmunocytopenia, Goodpasture's syndrome, Pemphigus vulgaris, myasthenia gravis, Grave's disease (hyperthyroidism), and insulin-resistant diabetes mellitus.

[0465] Additional disorders that are likely to have an autoimmune component that may be treated, prevented, and/or diagnosed with the compositions of the invention include, but are not limited to, type II collagen-induced arthritis, antiphospholipid syndrome, dermatitis, allergic encephalomyelitis, myocarditis, relapsing polychondritis, rheumatic heart disease, neuritis, uveitis ophthalmia, polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome, autoimmune pulmonary inflammation, autism, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disorders.

[0466] Additional disorders that are likely to have an autoimmune component that may be treated, prevented, diagnosed and/or prognosed with the compositions of the invention include, but are not limited to, scleroderma with anti-collagen antibodies (often

characterized, e.g., by nucleolar and other nuclear antibodies), mixed connective tissue disease (often characterized, e.g., by antibodies to extractable nuclear antigens (e.g., ribonucleoprotein)), polymyositis (often characterized, e.g., by nonhistone ANA), pernicious anemia (often characterized, e.g., by antiparietal cell, microsomes, and intrinsic factor antibodies), idiopathic Addison's disease (often characterized, e.g., by humoral and cell-mediated adrenal cytotoxicity, infertility (often characterized, e.g., by antispermatozoal antibodies), glomerulonephritis (often characterized, e.g., by glomerular basement membrane antibodies or immune complexes), bullous pemphigoid (often characterized, e.g., by IgG and complement in basement membrane), Sjogren's syndrome (often characterized, e.g., by multiple tissue antibodies, and/or a specific nonhistone ANA (SS-B)), diabetes mellitus (often characterized, e.g., by cell-mediated and humoral islet cell antibodies), and adrenergic drug resistance (including adrenergic drug resistance with asthma or cystic fibrosis) (often characterized, e.g., by beta-adrenergic receptor antibodies).

[0467] Additional disorders that may have an autoimmune component that may be treated, prevented, diagnosed and/or prognosed with the compositions of the invention include, but are not limited to, chronic active hepatitis (often characterized, e.g., by smooth muscle antibodies), primary biliary cirrhosis (often characterized, e.g., by mitochondria antibodies), other endocrine gland failure (often characterized, e.g., by specific tissue antibodies in some cases), vitiligo (often characterized, e.g., by melanocyte antibodies), vasculitis (often characterized, e.g., by Ig and complement in vessel walls and/or low serum complement), post-MI (often characterized, e.g., by myocardial antibodies), cardiomyopathy syndrome (often characterized, e.g., by myocardial antibodies), urticaria (often characterized, e.g., by IgG and IgM antibodies to IgE), atopic dermatitis (often characterized, e.g., by IgG and IgM antibodies to IgE), asthma (often characterized, e.g., by IgG and IgM antibodies to IgE), and many other inflammatory, granulomatous, degenerative, and atrophic disorders.

[0468] In a preferred embodiment, the autoimmune diseases and disorders and/or conditions associated with the diseases and disorders recited above are treated, prevented, diagnosed and/or prognosed using for example, antagonists or agonists, polypeptides or polynucleotides, or antibodies of the present invention. In a specific preferred

embodiment, rheumatoid arthritis is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

[0469] In another specific preferred embodiment, systemic lupus erythematosus is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention. In another specific preferred embodiment, idiopathic thrombocytopenia purpura is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

[0470] In another specific preferred embodiment IgA nephropathy is treated, prevented, and/or diagnosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

[0471] In a preferred embodiment, the autoimmune diseases and disorders and/or conditions associated with the diseases and disorders recited above are treated, prevented, diagnosed and/or prognosed using polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention.

[0472] In preferred embodiments, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a immunosuppressive agent(s).

[0473] Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, prognosing, and/or diagnosing diseases, disorders, and/or conditions of hematopoietic cells. Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat or prevent those diseases, disorders, and/or conditions associated with a decrease in certain (or many) types hematopoietic cells, including but not limited to, leukopenia, neutropenia, anemia, and thrombocytopenia. Alternatively, Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat or prevent those diseases, disorders, and/or conditions associated with an increase in certain (or many) types of hematopoietic cells, including but not limited to, histiocytosis.

[0474] Allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated, prevented, diagnosed and/or prognosed using polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof. Moreover, these molecules can be used to treat, prevent, prognose, and/or diagnose anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

[0475] Additionally, polypeptides or polynucleotides of the invention, and/or agonists or antagonists thereof, may be used to treat, prevent, diagnose and/or prognose IgE-mediated allergic reactions. Such allergic reactions include, but are not limited to, asthma, rhinitis, and eczema. In specific embodiments, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to modulate IgE concentrations in vitro or in vivo.

[0476] Moreover, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention have uses in the diagnosis, prognosis, prevention, and/or treatment of inflammatory conditions. For example, since polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists of the invention may inhibit the activation, proliferation and/or differentiation of cells involved in an inflammatory response, these molecules can be used to prevent and/or treat chronic and acute inflammatory conditions. Such inflammatory conditions include, but are not limited to, for example, inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome), ischemia-reperfusion injury, endotoxin lethality, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, over production of cytokines (e.g., TNF or IL-1.), respiratory disorders (e.g., asthma and allergy); gastrointestinal disorders (e.g., inflammatory bowel disease); cancers (e.g., gastric, ovarian, lung, bladder, liver, and breast); CNS disorders (e.g., multiple sclerosis; ischemic brain injury and/or stroke, traumatic brain injury, neurodegenerative disorders (e.g., Parkinson's disease and Alzheimer's disease); AIDS-related dementia; and prion disease); cardiovascular disorders (e.g., atherosclerosis, myocarditis, cardiovascular disease, and cardiopulmonary bypass complications); as well as many additional diseases, conditions, and disorders that are characterized by inflammation (e.g., hepatitis, rheumatoid arthritis,



gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal ischemia-reperfusion injury, Grave's disease, systemic lupus erythematosus, diabetes mellitus, and allogenic transplant rejection).

[0477] Because inflammation is a fundamental defense mechanism, inflammatory disorders can effect virtually any tissue of the body. Accordingly, polynucleotides, polypeptides, and antibodies of the invention, as well as agonists or antagonists thereof, have uses in the treatment of tissue-specific inflammatory disorders, including, but not limited to, adrenalitis, alveolitis, angiocholecystitis, appendicitis, balanitis, blepharitis, bronchitis, bursitis, carditis, cellulitis, cervicitis, cholecystitis, chorditis, cochitis, colitis, conjunctivitis, cystitis, dermatitis, diverticulitis, encephalitis, endocarditis, esophagitis, eustachitis, fibrositis, folliculitis, gastritis, gastroenteritis, gingivitis, glossitis, hepatosplenitis, keratitis, labyrinthitis, laryngitis, lymphangitis, mastitis, media otitis, meningitis, metritis, mucitis, myocarditis, myositis, myringitis, nephritis, neuritis, orchitis, osteochondritis, otitis, pericarditis, peritendonitis, peritonitis, pharyngitis, phlebitis, poliomyelitis, prostatitis, pulpitis, retinitis, rhinitis, salpingitis, scleritis, sclerochoroiditis, scrotitis, sinusitis, spondylitis, steatitis, stomatitis, synovitis, syringitis, tendonitis, tonsillitis, urethritis, and vaginitis.

[0478] In specific embodiments, polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, are useful to diagnose, prognose, prevent, and/or treat organ transplant rejections and graft-versus-host disease. Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. Polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, that inhibit an immune response, particularly the activation, proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD. In specific embodiments, polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, that inhibit an immune response, particularly the activation, proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing experimental allergic and hyperacute xenograft rejection.

[0479] In other embodiments, polypeptides, antibodies, or polynucleotides of the invention, and/or agonists or antagonists thereof, are useful to diagnose, prognose, prevent, and/or treat immune complex diseases, including, but not limited to, serum sickness, post streptococcal glomerulonephritis, polyarteritis nodosa, and immune complex-induced vasculitis.

[0480] Polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the invention can be used to treat, detect, and/or prevent infectious agents. For example, by increasing the immune response, particularly increasing the proliferation activation and/or differentiation of B and/or T cells, infectious diseases may be treated, detected, and/or prevented. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may also directly inhibit the infectious agent (refer to section of application listing infectious agents, etc), without necessarily eliciting an immune response.

[0481] In another embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a vaccine adjuvant that enhances immune responsiveness to an antigen. In a specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance tumor-specific immune responses.

[0482] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance anti-viral immune responses. Anti-viral immune responses that may be enhanced using the compositions of the invention as an adjuvant, include virus and virus associated diseases or symptoms described herein or otherwise known in the art. In specific embodiments, the compositions of the invention are used as an adjuvant to enhance an immune response to a virus, disease, or symptom selected from the group consisting of: AIDS, meningitis, Dengue, EBV, and hepatitis (e.g., hepatitis B). In another specific embodiment, the compositions of the invention are used as an adjuvant to enhance an immune response to a virus, disease, or symptom selected from the group consisting of: HIV/AIDS, respiratory syncytial virus, Dengue, rotavirus, Japanese B encephalitis,

influenza A and B, parainfluenza, measles, cytomegalovirus, rabies, Junin, Chikungunya, Rift Valley Fever, herpes simplex, and yellow fever.

[0483] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance anti-bacterial or anti-fungal immune responses. Anti-bacterial or anti-fungal immune responses that may be enhanced using the compositions of the invention as an adjuvant, include bacteria or fungus and bacteria or fungus associated diseases or symptoms described herein or otherwise known in the art. In specific embodiments, the compositions of the invention are used as an adjuvant to enhance an immune response to a bacteria or fungus, disease, or symptom selected from the group consisting of: tetanus, Diphtheria, botulism, and meningitis type B.

[0484] In another specific embodiment, the compositions of the invention are used as an adjuvant to enhance an immune response to a bacteria or fungus, disease, or symptom selected from the group consisting of: *Vibrio cholerae*, *Mycobacterium leprae*, *Salmonella typhi*, *Salmonella paratyphi*, *Meisseria meningitidis*, *Streptococcus pneumoniae*, Group B streptococcus, *Shigella spp.*, Enterotoxigenic *Escherichia coli*, Enterohemorrhagic *E. coli*, and *Borrelia burgdorferi*.

[0485] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an adjuvant to enhance anti-parasitic immune responses. Anti-parasitic immune responses that may be enhanced using the compositions of the invention as an adjuvant, include parasite and parasite associated diseases or symptoms described herein or otherwise known in the art. In specific embodiments, the compositions of the invention are used as an adjuvant to enhance an immune response to a parasite. In another specific embodiment, the compositions of the invention are used as an adjuvant to enhance an immune response to Plasmodium (malaria) or Leishmania.

[0486] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may also be employed to treat infectious diseases including silicosis, sarcoidosis, and idiopathic pulmonary fibrosis; for example, by preventing the recruitment and activation of mononuclear phagocytes.

[0487] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an antigen for the generation of antibodies to inhibit or enhance immune mediated responses against polypeptides of the invention.

[0488] In one embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are administered to an animal (e.g., mouse, rat, rabbit, hamster, guinea pig, pigs, micro-pig, chicken, camel, goat, horse, cow, sheep, dog, cat, non-human primate, and human, most preferably human) to boost the immune system to produce increased quantities of one or more antibodies (e.g., IgG, IgA, IgM, and IgE), to induce higher affinity antibody production and immunoglobulin class switching (e.g., IgG, IgA, IgM, and IgE), and/or to increase an immune response.

[0489] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a stimulator of B cell responsiveness to pathogens.

[0490] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an activator of T cells.

[0491] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent that elevates the immune status of an individual prior to their receipt of immunosuppressive therapies.

[0492] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to induce higher affinity antibodies.

[0493] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to increase serum immunoglobulin concentrations.

[0494] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to accelerate recovery of immunocompromised individuals.

[0495] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to boost immunoresponsiveness among aged populations and/or neonates.

[0496] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an immune system enhancer prior to, during, or after bone marrow transplant and/or other transplants (e.g., allogeneic or xenogeneic organ transplantation). With respect to transplantation, compositions of the invention may be administered prior to, concomitant with, and/or after transplantation. In a specific embodiment, compositions of the invention are administered after transplantation, prior to the beginning of recovery of T-cell populations. In another specific embodiment, compositions of the invention are first administered after transplantation after the beginning of recovery of T cell populations, but prior to full recovery of B cell populations.

[0497] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to boost immunoresponsiveness among individuals having an acquired loss of B cell function. Conditions resulting in an acquired loss of B cell function that may be ameliorated or treated by administering the polypeptides, antibodies, polynucleotides and/or agonists or antagonists thereof, include, but are not limited to, HIV Infection, AIDS, bone marrow transplant, and B cell chronic lymphocytic leukemia (CLL).

[0498] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to boost immunoresponsiveness among individuals having a temporary immune deficiency. Conditions resulting in a temporary immune deficiency that may be ameliorated or treated by administering the polypeptides, antibodies, polynucleotides and/or agonists or antagonists thereof, include, but are not limited to, recovery from viral infections (e.g., influenza), conditions associated with malnutrition, recovery from infectious mononucleosis, or conditions associated with stress, recovery from measles, recovery from blood transfusion, and recovery from surgery.

[0499] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a regulator of antigen presentation by monocytes, dendritic cells, and/or B-cells. In one embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention enhance antigen presentation or antagonizes antigen presentation in vitro or in

vivo. Moreover, in related embodiments, said enhancement or antagonism of antigen presentation may be useful as an anti-tumor treatment or to modulate the immune system.

[0500] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an agent to direct an individual's immune system towards development of a humoral response (i.e. TH2) as opposed to a TH1 cellular response.

[0501] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means to induce tumor proliferation and thus make it more susceptible to anti-neoplastic agents. For example, multiple myeloma is a slowly dividing disease and is thus refractory to virtually all anti-neoplastic regimens. If these cells were forced to proliferate more rapidly their susceptibility profile would likely change.

[0502] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a stimulator of B cell production in pathologies such as AIDS, chronic lymphocyte disorder and/or Common Variable Immunodeficiency.

[0503] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for generation and/or regeneration of lymphoid tissues following surgery, trauma or genetic defect. In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used in the pretreatment of bone marrow samples prior to transplant.

[0504] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a gene-based therapy for genetically inherited disorders resulting in immuno-incompetence/immunodeficiency such as observed among SCID patients.

[0505] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of activating monocytes/macrophages to defend against parasitic diseases that effect monocytes such as Leishmania.

[0506] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of regulating secreted cytokines that are elicited by polypeptides of the invention.

[0507] In another embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used in one or more of the applications described herein, as they may apply to veterinary medicine.

[0508] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of blocking various aspects of immune responses to foreign agents or self. Examples of diseases or conditions in which blocking of certain aspects of immune responses may be desired include autoimmune disorders such as lupus, and arthritis, as well as immunoresponsiveness to skin allergies, inflammation, bowel disease, injury and diseases/disorders associated with pathogenesis.

[0509] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for preventing the B cell proliferation and Ig secretion associated with autoimmune diseases such as idiopathic thrombocytopenic purpura, systemic lupus erythematosus and multiple sclerosis.

[0510] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as an inhibitor of B and/or T cell migration in endothelial cells. This activity disrupts tissue architecture or cognate responses and is useful, for example in disrupting immune responses, and blocking sepsis.

[0511] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for chronic hypergammaglobulinemia evident in such diseases as monoclonal gammopathy of undetermined significance (MGUS), Waldenstrom's disease, related idiopathic monoclonal gammopathies, and plasmacytomas.

[0512] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be employed for instance to inhibit polypeptide chemotaxis and activation of macrophages and their precursors, and of neutrophils, basophils, B lymphocytes and some T-cell subsets, e.g., activated and CD8

cytotoxic T cells and natural killer cells, in certain autoimmune and chronic inflammatory and infective diseases. Examples of autoimmune diseases are described herein and include multiple sclerosis, and insulin-dependent diabetes.

[0513] The polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may also be employed to treat idiopathic hyper-eosinophilic syndrome by, for example, preventing eosinophil production and migration.

[0514] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used to enhance or inhibit complement mediated cell lysis.

[0515] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used to enhance or inhibit antibody dependent cellular cytotoxicity.

[0516] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may also be employed for treating atherosclerosis, for example, by preventing monocyte infiltration in the artery wall.

[0517] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be employed to treat adult respiratory distress syndrome (ARDS).

[0518] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be useful for stimulating wound and tissue repair, stimulating angiogenesis, and/or stimulating the repair of vascular or lymphatic diseases or disorders. Additionally, agonists and antagonists of the invention may be used to stimulate the regeneration of mucosal surfaces.

[0519] In a specific embodiment, polynucleotides or polypeptides, and/or agonists thereof are used to diagnose, prognose, treat, and/or prevent a disorder characterized by primary or acquired immunodeficiency, deficient serum immunoglobulin production, recurrent infections, and/or immune system dysfunction. Moreover, polynucleotides or polypeptides, and/or agonists thereof may be used to treat or prevent infections of the joints, bones, skin, and/or parotid glands, blood-borne infections (e.g., sepsis, meningitis, septic arthritis, and/or osteomyelitis), autoimmune diseases (e.g., those disclosed herein), inflammatory disorders, and malignancies, and/or any disease or disorder or condition



associated with these infections, diseases, disorders and/or malignancies) including, but not limited to, CVID, other primary immune deficiencies, HIV disease, CLL, recurrent bronchitis, sinusitis, otitis media, conjunctivitis, pneumonia, hepatitis, meningitis, herpes zoster (e.g., severe herpes zoster), and/or pneumocystis carinii. Other diseases and disorders that may be prevented, diagnosed, prognosed, and/or treated with polynucleotides or polypeptides, and/or agonists of the present invention include, but are not limited to, HIV infection, HTLV-BLV infection, lymphopenia, phagocyte bactericidal dysfunction anemia, thrombocytopenia, and hemoglobinuria.

[0520] In another embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention are used to treat, and/or diagnose an individual having common variable immunodeficiency disease ("CVID"; also known as "acquired agammaglobulinemia" and "acquired hypogammaglobulinemia") or a subset of this disease.

[0521] In a specific embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to diagnose, prognose, prevent, and/or treat cancers or neoplasms including immune cell or immune tissue-related cancers or neoplasms. Examples of cancers or neoplasms that may be prevented, diagnosed, or treated by polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include, but are not limited to, acute myelogenous leukemia, chronic myelogenous leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic anemia (ALL) Chronic lymphocyte leukemia, plasmacytomas, multiple myeloma, Burkitt's lymphoma, EBV-transformed diseases, and/or diseases and disorders described in the section entitled "Hyperproliferative Disorders" elsewhere herein.

[0522] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a therapy for decreasing cellular proliferation of Large B-cell Lymphomas.

[0523] In another specific embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are used as a means of decreasing the involvement of B cells and Ig associated with Chronic Myelogenous Leukemia.

[0524] In specific embodiments, the compositions of the invention are used as an agent to boost immunoresponsiveness among B cell immunodeficient individuals, such as, for example, an individual who has undergone a partial or complete splenectomy.

[0525] Antagonists of the invention include, for example, binding and/or inhibitory antibodies, antisense nucleic acids, ribozymes or soluble forms of the polypeptides of the present invention (e.g., Fc fusion protein; see, e.g., Example 9). Agonists of the invention include, for example, binding or stimulatory antibodies, and soluble forms of the polypeptides (e.g., Fc fusion proteins; see, e.g., Example 9). Polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention may be employed in a composition with a pharmaceutically acceptable carrier, e.g., as described herein.

[0526] In another embodiment, polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention are administered to an animal (including, but not limited to, those listed above, and also including transgenic animals) incapable of producing functional endogenous antibody molecules or having an otherwise compromised endogenous immune system, but which is capable of producing human immunoglobulin molecules by means of a reconstituted or partially reconstituted immune system from another animal (see, e.g., published PCT Application Nos. WO98/24893, WO/9634096, WO/9633735, and WO/9110741). Administration of polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention to such animals is useful for the generation of monoclonal antibodies against the polypeptides, antibodies, polynucleotides and/or agonists or antagonists of the present invention.

#### **Blood-Related Disorders**

[0527] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to modulate hemostatic (the stopping of bleeding) or thrombolytic (clot dissolving) activity. For example, by increasing hemostatic or thrombolytic activity, polynucleotides or polypeptides, and/or agonists or antagonists of the present invention could be used to treat or prevent blood coagulation diseases, disorders, and/or conditions (e.g., afibrinogenemia, factor deficiencies, hemophilia), blood platelet diseases, disorders, and/or conditions (e.g., thrombocytopenia),

or wounds resulting from trauma, surgery, or other causes. Alternatively, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment or prevention of heart attacks (infarction), strokes, or scarring.

[0528] In specific embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to prevent, diagnose, prognose, and/or treat thrombosis, arterial thrombosis, venous thrombosis, thromboembolism, pulmonary embolism, atherosclerosis, myocardial infarction, transient ischemic attack, unstable angina. In specific embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used for the prevention of occlusion of saphenous grafts, for reducing the risk of periprocedural thrombosis as might accompany angioplasty procedures, for reducing the risk of stroke in patients with atrial fibrillation including nonrheumatic atrial fibrillation, for reducing the risk of embolism associated with mechanical heart valves and or mitral valves disease. Other uses for the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention, include, but are not limited to, the prevention of occlusions in extracorporeal devices (e.g., intravascular canulas, vascular access shunts in hemodialysis patients, hemodialysis machines, and cardiopulmonary bypass machines).

[0529] In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to prevent, diagnose, prognose, and/or treat diseases and disorders of the blood and/or blood forming organs associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1, column 7 (Tissue Distribution Library Code).

[0530] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to modulate hematopoietic activity (the formation of blood cells). For example, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to increase the quantity of all or subsets of blood cells, such as, for example, erythrocytes, lymphocytes

(B or T cells), myeloid cells (e.g., basophils, eosinophils, neutrophils, mast cells, macrophages) and platelets. The ability to decrease the quantity of blood cells or subsets of blood cells may be useful in the prevention, detection, diagnosis and/or treatment of anemias and leukopenias described below. Alternatively, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to decrease the quantity of all or subsets of blood cells, such as, for example, erythrocytes, lymphocytes (B or T cells), myeloid cells (e.g., basophils, eosinophils, neutrophils, mast cells, macrophages) and platelets. The ability to decrease the quantity of blood cells or subsets of blood cells may be useful in the prevention, detection, diagnosis and/or treatment of leukocytoses, such as, for example eosinophilia.

[0531] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be used to prevent, treat, or diagnose blood dyscrasia.

[0532] Anemias are conditions in which the number of red blood cells or amount of hemoglobin (the protein that carries oxygen) in them is below normal. Anemia may be caused by excessive bleeding, decreased red blood cell production, or increased red blood cell destruction (hemolysis). The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, and/or diagnosing anemias. Anemias that may be treated prevented or diagnosed by the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include iron deficiency anemia, hypochromic anemia, microcytic anemia, chlorosis, hereditary sideroblastic anemia, idiopathic acquired sideroblastic anemia, red cell aplasia, megaloblastic anemia (e.g., pernicious anemia, (vitamin B12 deficiency) and folic acid deficiency anemia), aplastic anemia, hemolytic anemias (e.g., autoimmune hemolytic anemia, microangiopathic hemolytic anemia, and paroxysmal nocturnal hemoglobinuria). The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, and/or diagnosing anemias associated with diseases including but not limited to, anemias associated with systemic lupus erythematosus, cancers, lymphomas, chronic renal disease, and enlarged spleens. The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, and/or

diagnosing anemias arising from drug treatments such as anemias associated with methyl dopa, dapsone, and/or sulfadiazine. Additionally, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, and/or diagnosing anemias associated with abnormal red blood cell architecture including but not limited to, hereditary spherocytosis, hereditary elliptocytosis, glucose-6-phosphate dehydrogenase deficiency, and sickle cell anemia.

[0533] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, and/or diagnosing hemoglobin abnormalities, (e.g., those associated with sickle cell anemia, hemoglobin C disease, hemoglobin S-C disease, and hemoglobin E disease). Additionally, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating thalassemias, including, but not limited to major and minor forms of alpha-thalassemia and beta-thalassemia.

[0534] In another embodiment, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating bleeding disorders including, but not limited to, thrombocytopenia (e.g., idiopathic thrombocytopenic purpura, and thrombotic thrombocytopenic purpura), Von Willebrand's disease, hereditary platelet disorders (e.g., storage pool disease such as Chediak-Higashi and Hermansky-Pudlak syndromes, thromboxane A<sub>2</sub> dysfunction, thromboasthenia, and Bernard-Soulier syndrome), hemolytic-uremic syndrome, hemophelias such as hemophilia A or Factor VII deficiency and Christmas disease or Factor IX deficiency, Hereditary Hemorrhagic Telangiectasia, also known as Rendu-Osler-Weber syndrome, allergic purpura (Henoch Schonlein purpura) and disseminated intravascular coagulation.

[0535] The effect of the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention on the clotting time of blood may be monitored using any of the clotting tests known in the art including, but not limited to, whole blood partial thromboplastin time (PTT), the activated partial thromboplastin time (aPTT), the activated clotting time (ACT), the recalcified activated clotting time, or the Lee-White Clotting time.

[0536] Several diseases and a variety of drugs can cause platelet dysfunction. Thus, in a specific embodiment, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating acquired platelet dysfunction such as platelet dysfunction accompanying kidney failure, leukemia, multiple myeloma, cirrhosis of the liver, and systemic lupus erythematosus as well as platelet dysfunction associated with drug treatments, including treatment with aspirin, ticlopidine, nonsteroidal anti-inflammatory drugs (used for arthritis, pain, and sprains), and penicillin in high doses.

[0537] In another embodiment, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating diseases and disorders characterized by or associated with increased or decreased numbers of white blood cells. Leukopenia occurs when the number of white blood cells decreases below normal. Leukopenias include, but are not limited to, neutropenia and lymphocytopenia. An increase in the number of white blood cells compared to normal is known as leukocytosis. The body generates increased numbers of white blood cells during infection. Thus, leukocytosis may simply be a normal physiological parameter that reflects infection. Alternatively, leukocytosis may be an indicator of injury or other disease such as cancer. Leukocytoses, include but are not limited to, eosinophilia, and accumulations of macrophages. In specific embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating leukopenia. In other specific embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating leukocytosis.

[0538] Leukopenia may be a generalized decrease in all types of white blood cells, or may be a specific depletion of particular types of white blood cells. Thus, in specific embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating decreases in neutrophil numbers, known as neutropenia. Neutropenias that may be diagnosed, prognosed, prevented, and/or treated by the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention include,

but are not limited to, infantile genetic agranulocytosis, familial neutropenia, cyclic neutropenia, neutropenias resulting from or associated with dietary deficiencies (e.g., vitamin B 12 deficiency or folic acid deficiency), neutropenias resulting from or associated with drug treatments (e.g., antibiotic regimens such as penicillin treatment, sulfonamide treatment, anticoagulant treatment, anticonvulsant drugs, anti-thyroid drugs, and cancer chemotherapy), and neutropenias resulting from increased neutrophil destruction that may occur in association with some bacterial or viral infections, allergic disorders, autoimmune diseases, conditions in which an individual has an enlarged spleen (e.g., Felty syndrome, malaria and sarcoidosis), and some drug treatment regimens.

[0539] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating lymphocytopenias (decreased numbers of B and/or T lymphocytes), including, but not limited lymphocytopenias resulting from or associated with stress, drug treatments (e.g., drug treatment with corticosteroids, cancer chemotherapies, and/or radiation therapies), AIDS infection and/or other diseases such as, for example, cancer, rheumatoid arthritis, systemic lupus erythematosus, chronic infections, some viral infections and/or hereditary disorders (e.g., DiGeorge syndrome, Wiskott-Aldrich Syndrome, severe combined immunodeficiency, ataxia telangiectasia).

[0540] The polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating diseases and disorders associated with macrophage numbers and/or macrophage function including, but not limited to, Gaucher's disease, Niemann-Pick disease, Letterer-Siwe disease and Hand-Schuller-Christian disease.

[0541] In another embodiment, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating diseases and disorders associated with eosinophil numbers and/or eosinophil function including, but not limited to, idiopathic hypereosinophilic syndrome, eosinophilia-myalgia syndrome, and Hand-Schuller-Christian disease.

[0542] In yet another embodiment, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing,

prognosing, preventing, and/or treating leukemias and lymphomas including, but not limited to, acute lymphocytic (lymphoblastic) leukemia (ALL), acute myeloid (myelocytic, myelogenous, myeloblastic, or myelomonocytic) leukemia, chronic lymphocytic leukemia (e.g., B cell leukemias, T cell leukemias, Sezary syndrome, and Hairy cell leukemia), chronic myelocytic (myeloid, myelogenous, or granulocytic) leukemia, Hodgkin's lymphoma, non-hodgkin's lymphoma, Burkitt's lymphoma, and mycosis fungoides.

[0543] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in diagnosing, prognosing, preventing, and/or treating diseases and disorders of plasma cells including, but not limited to, plasma cell dyscrasias, monoclonal gammaopathies, monoclonal gammopathies of undetermined significance, multiple myeloma, macroglobulinemia, Waldenstrom's macroglobulinemia, cryoglobulinemia, and Raynaud's phenomenon.

[0544] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in treating, preventing, and/or diagnosing myeloproliferative disorders, including but not limited to, polycythemia vera, relative polycythemia, secondary polycythemia, myelofibrosis, acute myelofibrosis, agnogenic myeloid metaplasia, thrombocythemia, (including both primary and secondary thrombocythemia) and chronic myelocytic leukemia.

[0545] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful as a treatment prior to surgery, to increase blood cell production.

[0546] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful as an agent to enhance the migration, phagocytosis, superoxide production, antibody dependent cellular cytotoxicity of neutrophils, eosinophils and macrophages.

[0547] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful as an agent to increase the number of stem cells in circulation prior to stem cells pheresis. In another specific embodiment, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists



of the present invention may be useful as an agent to increase the number of stem cells in circulation prior to platelet pheresis.

[0548] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful as an agent to increase cytokine production.

[0549] In other embodiments, the polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention may be useful in preventing, diagnosing, and/or treating primary hematopoietic disorders.

### **Hyperproliferative Disorders**

[0550] Ovarian associated polynucleotides or polypeptides, or agonists or antagonists thereof, can be used to treat, prevent, diagnose and/or prognose hyperproliferative diseases, disorders, and/or conditions, including neoplasms.

[0551] In a specific embodiment, ovarian associated polynucleotides or polypeptides, or agonists or antagonists thereof, can be used to treat, prevent, and/or diagnose hyperproliferative diseases, disorders, and/or conditions of the breast and ovaries.

[0552] In a preferred embodiment, ovarian associated polynucleotides or polypeptides, or agonists or antagonists thereof, can be used to treat, prevent, and/or diagnose breast and ovarian neoplasms.

[0553] Ovarian associated polynucleotides or polypeptides, or agonists or antagonists of the invention, may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, ovarian associated polynucleotides or polypeptides, or agonists or antagonists thereof, may proliferate other cells, which can inhibit the hyperproliferative disorder.

[0554] For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative diseases, disorders, and/or conditions can be treated, prevented, and/or diagnosed. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating,

preventing, and/or diagnosing hyperproliferative diseases, disorders, and/or conditions, such as a chemotherapeutic agent.

[0555] Examples of hyperproliferative diseases, disorders, and/or conditions that can be treated, prevented, and/or diagnosed by ovarian associated polynucleotides or polypeptides, or agonists or antagonists thereof, include, but are not limited to neoplasms located in the: prostate, colon, abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

[0556] Similarly, other hyperproliferative disorders can also be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: Acute Childhood Lymphoblastic Leukemia, Acute Lymphoblastic Leukemia, Acute Lymphocytic Leukemia, Acute Myeloid Leukemia, Adrenocortical Carcinoma, Adult (Primary) Hepatocellular Cancer, Adult (Primary) Liver Cancer, Adult Acute Lymphocytic Leukemia, Adult Acute Myeloid Leukemia, Adult Hodgkin's Disease, Adult Hodgkin's Lymphoma, Adult Lymphocytic Leukemia, Adult Non-Hodgkin's Lymphoma, Adult Primary Liver Cancer, Adult Soft Tissue Sarcoma, AIDS-Related Lymphoma, AIDS-Related Malignancies, Anal Cancer, Astrocytoma, Bile Duct Cancer, Bladder Cancer, Bone Cancer, Brain Stem Glioma, Brain Tumors, Breast Cancer, Cancer of the Renal Pelvis and Ureter, Central Nervous System (Primary) Lymphoma, Central Nervous System Lymphoma, Cerebellar Astrocytoma, Cerebral Astrocytoma, Cervical Cancer, Childhood (Primary) Hepatocellular Cancer, Childhood (Primary) Liver Cancer, Childhood Acute Lymphoblastic Leukemia, Childhood Acute Myeloid Leukemia, Childhood Brain Stem Glioma, Childhood Cerebellar Astrocytoma, Childhood Cerebral Astrocytoma, Childhood Extracranial Germ Cell Tumors, Childhood Hodgkin's Disease, Childhood Hodgkin's Lymphoma, Childhood Hypothalamic and Visual Pathway Glioma, Childhood Lymphoblastic Leukemia, Childhood Medulloblastoma, Childhood Non-Hodgkin's Lymphoma, Childhood Pineal and Supratentorial Primitive Neuroectodermal Tumors, Childhood Primary Liver Cancer, Childhood Rhabdomyosarcoma, Childhood Soft Tissue Sarcoma, Childhood Visual Pathway and Hypothalamic Glioma, Chronic

Lymphocytic Leukemia, Chronic Myelogenous Leukemia, Colon Cancer, Cutaneous T-Cell Lymphoma, Endocrine Pancreas Islet Cell Carcinoma, Endometrial Cancer, Ependymoma, Epithelial Cancer, Esophageal Cancer, Ewing's Sarcoma and Related Tumors, Exocrine Pancreatic Cancer, Extracranial Germ Cell Tumor, Extragonadal Germ Cell Tumor, Extrahepatic Bile Duct Cancer, Eye Cancer, Female Breast Cancer, Gaucher's Disease, Gallbladder Cancer, Gastric Cancer, Gastrointestinal Carcinoid Tumor, Gastrointestinal Tumors, Germ Cell Tumors, Gestational Trophoblastic Tumor, Hairy Cell Leukemia, Head and Neck Cancer, Hepatocellular Cancer, Hodgkin's Disease, Hodgkin's Lymphoma, Hypergammaglobulinemia, Hypopharyngeal Cancer, Intestinal Cancers, Intraocular Melanoma, Islet Cell Carcinoma, Islet Cell Pancreatic Cancer, Kaposi's Sarcoma, Kidney Cancer, Laryngeal Cancer, Lip and Oral Cavity Cancer, Liver Cancer, Lung Cancer, Lymphoproliferative Disorders, Macroglobulinemia, Male Breast Cancer, Malignant Mesothelioma, Malignant Thymoma, Medulloblastoma, Melanoma, Mesothelioma, Metastatic Occult Primary Squamous Neck Cancer, Metastatic Primary Squamous Neck Cancer, Metastatic Squamous Neck Cancer, Multiple Myeloma, Multiple Myeloma/Plasma Cell Neoplasm, Myelodysplastic Syndrome, Myelogenous Leukemia, Myeloid Leukemia, Myeloproliferative Disorders, Nasal Cavity and Paranasal Sinus Cancer, Nasopharyngeal Cancer, Neuroblastoma, Non-Hodgkin's Lymphoma During Pregnancy, Nonmelanoma Skin Cancer, Non-Small Cell Lung Cancer, Occult Primary Metastatic Squamous Neck Cancer, Oropharyngeal Cancer, Osteo-/Malignant Fibrous Sarcoma, Osteosarcoma/Malignant Fibrous Histiocytoma, Osteosarcoma/Malignant Fibrous Histiocytoma of Bone, Ovarian Epithelial Cancer, Ovarian Germ Cell Tumor, Ovarian Low Malignant Potential Tumor, Pancreatic Cancer, Paraproteinemias, Purpura, Parathyroid Cancer, Penile Cancer, Pheochromocytoma, Pituitary Tumor, Plasma Cell Neoplasm/Multiple Myeloma, Primary Central Nervous System Lymphoma, Primary Liver Cancer, Prostate Cancer, Rectal Cancer, Renal Cell Cancer, Renal Pelvis and Ureter Cancer, Retinoblastoma, Rhabdomyosarcoma, Salivary Gland Cancer, Sarcoidosis Sarcomas, Sezary Syndrome, Skin Cancer, Small Cell Lung Cancer, Small Intestine Cancer, Soft Tissue Sarcoma, Squamous Neck Cancer, Stomach Cancer, Supratentorial Primitive Neuroectodermal and Pineal Tumors, T-Cell Lymphoma, Testicular Cancer, Thymoma, Thyroid Cancer, Transitional Cell Cancer of the Renal Pelvis and Ureter,

Transitional Renal Pelvis and Ureter Cancer, Trophoblastic Tumors, Ureter and Renal Pelvis Cell Cancer, Urethral Cancer, Uterine Cancer, Uterine Sarcoma, Vaginal Cancer, Visual Pathway and Hypothalamic Glioma, Vulvar Cancer, Waldenstrom's Macroglobulinemia, Wilms' Tumor, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

[0557] In another preferred embodiment, polynucleotides or polypeptides, or agonists or antagonists of the present invention are used to diagnose, prognose, prevent, and/or treat premalignant conditions and to prevent progression to a neoplastic or malignant state, including but not limited to those disorders described above. Such uses are indicated in conditions known or suspected of preceding progression to neoplasia or cancer, in particular, where non-neoplastic cell growth consisting of hyperplasia, metaplasia, or most particularly, dysplasia has occurred (for review of such abnormal growth conditions, see Robbins and Angell, 1976, Basic Pathology, 2d.Ed., W. B. Saunders Co., Philadelphia, pp. 68-79.)

[0558] Hyperplasia is a form of controlled cell proliferation, involving an increase in cell number in a tissue or organ, without significant alteration in structure or function. Hyperplastic disorders which can be diagnosed, prognosed, prevented, and/or treated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, angiofollicular mediastinal lymph node hyperplasia, angiolymphoid hyperplasia with eosinophilia, atypical melanocytic hyperplasia, basal cell hyperplasia, benign giant lymph node hyperplasia, cementum hyperplasia, congenital adrenal hyperplasia, congenital sebaceous hyperplasia, cystic hyperplasia, cystic hyperplasia of the breast, denture hyperplasia, ductal hyperplasia, endometrial hyperplasia, fibromuscular hyperplasia, focal epithelial hyperplasia, gingival hyperplasia, inflammatory fibrous hyperplasia, inflammatory papillary hyperplasia, intravascular papillary endothelial hyperplasia, nodular hyperplasia of prostate, nodular regenerative hyperplasia, pseudoepitheliomatous hyperplasia, senile sebaceous hyperplasia, and verrucous hyperplasia.

[0559] Metaplasia is a form of controlled cell growth in which one type of adult or fully differentiated cell substitutes for another type of adult cell. Metaplastic disorders which can be diagnosed, prognosed, prevented, and/or treated with compositions of the

invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, agnogenic myeloid metaplasia, apocrine metaplasia, atypical metaplasia, autoparenchymatous metaplasia, connective tissue metaplasia, epithelial metaplasia, intestinal metaplasia, metaplastic anemia, metaplastic ossification, metaplastic polyps, myeloid metaplasia, primary myeloid metaplasia, secondary myeloid metaplasia, squamous metaplasia, squamous metaplasia of amnion, and symptomatic myeloid metaplasia.

[0560] Dysplasia is frequently a forerunner of cancer, and is found mainly in the epithelia; it is the most disorderly form of non-neoplastic cell growth, involving a loss in individual cell uniformity and in the architectural orientation of cells. Dysplastic cells often have abnormally large, deeply stained nuclei, and exhibit pleomorphism. Dysplasia characteristically occurs where there exists chronic irritation or inflammation. Dysplastic disorders which can be diagnosed, prognosed, prevented, and/or treated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, anhidrotic ectodermal dysplasia, anterofacial dysplasia, asphyxiating thoracic dysplasia, atriadigital dysplasia, bronchopulmonary dysplasia, cerebral dysplasia, cervical dysplasia, chondroectodermal dysplasia, cleidocranial dysplasia, congenital ectodermal dysplasia, craniodiaphysial dysplasia, craniocarpotarsal dysplasia, craniometaphysial dysplasia, dentin dysplasia, diaphysial dysplasia, ectodermal dysplasia, enamel dysplasia, encephalo-ophthalmic dysplasia, dysplasia epiphysialis hemimelia, dysplasia epiphysialis multiplex, dysplasia epiphysialis punctata, epithelial dysplasia, facioidigitogenital dysplasia, familial fibrous dysplasia of jaws, familial white folded dysplasia, fibromuscular dysplasia, fibrous dysplasia of bone, florid osseous dysplasia, hereditary renal-retinal dysplasia, hidrotic ectodermal dysplasia, hypohidrotic ectodermal dysplasia, lymphopenic thymic dysplasia, mammary dysplasia, mandibulofacial dysplasia, metaphysial dysplasia, Mondini dysplasia, monostotic fibrous dysplasia, mucoepithelial dysplasia, multiple epiphysial dysplasia, oculoauriculovertebral dysplasia, oculodentodigital dysplasia, oculovertbral dysplasia, odontogenic dysplasia, ophthalmomandibulomelic dysplasia, periapical cemental dysplasia, polyostotic fibrous dysplasia, pseudoachondroplastic spondyloepiphysial dysplasia, retinal dysplasia, septo-optic dysplasia, spondyloepiphysial dysplasia, and ventriculoradial dysplasia.

[0561] Additional pre-neoplastic disorders which can be diagnosed, prognosed, prevented, and/or treated with compositions of the invention (including polynucleotides, polypeptides, agonists or antagonists) include, but are not limited to, benign dysproliferative disorders (e.g., benign tumors, fibrocystic conditions, tissue hypertrophy, intestinal polyps, colon polyps, and esophageal dysplasia), leukoplakia, keratoses, Bowen's disease, Farmer's Skin, solar cheilitis, and solar keratosis.

[0562] In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to diagnose and/or prognose disorders associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1, 7 (Tissue Distribution Library Code).

[0563] In another embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention conjugated to a toxin or a radioactive isotope, as described herein, may be used to treat cancers and neoplasms, including, but not limited to those described herein. In a further preferred embodiment, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention conjugated to a toxin or a radioactive isotope, as described herein, may be used to treat acute myelogenous leukemia.

[0564] Additionally, polynucleotides, polypeptides, and/or agonists or antagonists of the invention may affect apoptosis, and therefore, would be useful in treating a number of diseases associated with increased cell survival or the inhibition of apoptosis. For example, diseases associated with increased cell survival or the inhibition of apoptosis that could be diagnosed, prognosed, prevented, and/or treated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's

disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection.

[0565] In preferred embodiments, polynucleotides, polypeptides, and/or agonists or antagonists of the invention are used to inhibit growth, progression, and/or metastasis of cancers, in particular those listed above.

[0566] Additional diseases or conditions associated with increased cell survival that could be diagnosed, prognosed, prevented, and/or treated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, emangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma, and retinoblastoma.

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15 7] 7] 7] 7] Diseases associated with increased apoptosis that could be diagnosed, prevented, and/or treated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) dysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestasis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

15 8] 8] 8] 8] Hyperproliferative diseases and/or disorders that could be diagnosed, prevented, and/or treated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention, include, but are not limited to, neoplasms located in the liver, bone, breast, digestive system, pancreas, peritoneum, endocrine glands (adrenal, thyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous system (central and peripheral), lymphatic system, pelvis, skin, soft tissue, spleen, thorax, and urogenital tract.

15 9] 9] 9] 9] Similarly, other hyperproliferative disorders can also be diagnosed, prevented, and/or treated by polynucleotides, polypeptides, and/or agonists or antagonists of the invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, autoimmune purpura, sarcoidosis, Sezary Syndrome, Waldenström's macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

15 0] 0] 0] 0] One preferred embodiment utilizes polynucleotides of the present invention to inhibit aberrant cellular division, by gene therapy using the present invention, and/or fusion or fragments thereof.



[0571] Thus, the present invention provides a method for treating cell proliferative diseases, disorders, and/or conditions by inserting into an abnormally proliferating cell a polynucleotide of the present invention, wherein said polynucleotide represses said cell proliferation, disease, disorder, and/or condition.

[0572] In a preferred embodiment, the present invention provides a method for treating cell proliferative diseases, disorders and/or conditions of the breast and ovaries by inserting into a cell, a polynucleotide of the present invention, wherein said polynucleotide represses said cell proliferation, disease and/or disorder.

[0573] Another embodiment of the present invention provides a method of treating cell-proliferative diseases, disorders, and/or conditions in individuals comprising administration of one or more active gene copies of the present invention to an abnormally proliferating cell or cells. In a preferred embodiment, polynucleotides of the present invention is a DNA construct comprising a recombinant expression vector effective in expressing a DNA sequence encoding said polynucleotides. In another preferred embodiment of the present invention, the DNA construct encoding the polynucleotides of the present invention is inserted into cells to be treated utilizing a retrovirus, or more preferably an adenoviral vector (see, e.g., G J. Nabel, et. al., PNAS 96: 324-326 (1999), which is hereby incorporated by reference). In a most preferred embodiment, the viral vector is defective and will not transform non-proliferating cells, only proliferating cells. Moreover, in a preferred embodiment, the polynucleotides of the present invention inserted into proliferating cells either alone, or in combination with or fused to other polynucleotides, can then be modulated via an external stimulus (i.e., magnetic, specific small molecule, chemical, or drug administration, etc.), which acts upon the promoter upstream of said polynucleotides to induce expression of the encoded protein product. As such the beneficial therapeutic affect of the present invention may be expressly modulated (i.e., to increase, decrease, or inhibit expression of the present invention) based upon said external stimulus.

[0574] Polynucleotides of the present invention may be useful in repressing expression of oncogenic genes or antigens. By "repressing expression of the oncogenic genes " is intended the suppression of the transcription of the gene, the degradation of the gene transcript (pre-message RNA), the inhibition of splicing, the destruction of the

messenger RNA, the prevention of the post-translational modifications of the protein, the destruction of the protein, or the inhibition of the normal function of the protein.

[0575] For local administration to abnormally proliferating cells, polynucleotides of the present invention may be administered by any method known to those of skill in the art including, but not limited to transfection, electroporation, microinjection of cells, or in vehicles such as liposomes, lipofectin, or as naked polynucleotides, or any other method described throughout the specification. The polynucleotide of the present invention may be delivered by known gene delivery systems such as, but not limited to, retroviral vectors (Gilboa, J. Virology 44:845 (1982); Hocke, Nature 320:275 (1986); Wilson, et al., Proc. Natl. Acad. Sci. U.S.A. 85:3014), vaccinia virus system (Chakrabarty et al., Mol. Cell Biol. 5:3403 (1985) or other efficient DNA delivery systems (Yates et al., Nature 313:812 (1985)) known to those skilled in the art. These references are exemplary only and are hereby incorporated by reference. In order to specifically deliver or transfect cells which are abnormally proliferating and spare non-dividing cells, it is preferable to utilize a retrovirus, or adenoviral (as described in the art and elsewhere herein) delivery system known to those of skill in the art. Since host DNA replication is required for retroviral DNA to integrate and the retrovirus will be unable to self-replicate due to the lack of the retrovirus genes needed for its life cycle. Utilizing such a retroviral delivery system for polynucleotides of the present invention will target said gene and constructs to abnormally proliferating cells and will spare the non-dividing normal cells.

[0576] The polynucleotides of the present invention may be delivered directly to cell proliferative disorder/disease sites in internal organs, body cavities and the like by use of imaging devices used to guide an injecting needle directly to the disease site. The polynucleotides of the present invention may also be administered to disease sites at the time of surgical intervention.

[0577] By "cell proliferative disease" is meant any human or animal disease or disorder, affecting any one or any combination of organs, cavities, or body parts, which is characterized by single or multiple local abnormal proliferations of cells, groups of cells, or tissues, whether benign or malignant.

[0578] Any amount of the polynucleotides of the present invention may be administered as long as it has a biologically inhibiting effect on the proliferation of the

treated cells. Moreover, it is possible to administer more than one of the polynucleotide of the present invention simultaneously to the same site. By "biologically inhibiting" is meant partial or total growth inhibition as well as decreases in the rate of proliferation or growth of the cells. The biologically inhibitory dose may be determined by assessing the effects of the polynucleotides of the present invention on target malignant or abnormally proliferating cell growth in tissue culture, tumor growth in animals and cell cultures, or any other method known to one of ordinary skill in the art.

[0579] The present invention is further directed to antibody-based therapies which involve administering of anti-polypeptides and anti-polynucleotide antibodies to a mammalian, preferably human, patient for treating one or more of the described diseases, disorders, and/or conditions. Methods for producing anti-polypeptides and anti-polynucleotide antibodies polyclonal and monoclonal antibodies are described in detail elsewhere herein. Such antibodies may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

[0580] A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g., as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

[0581] In particular, the antibodies, fragments and derivatives of the present invention are useful for treating a subject having or developing cell proliferative and/or differentiation diseases, disorders, and/or conditions as described herein. Such treatment comprises administering a single or multiple doses of the antibody, or a fragment, derivative, or a conjugate thereof.

[0582] The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors, for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

[0583] It is preferred to use high affinity and/or potent *in vivo* inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of diseases, disorders, and/or conditions related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides, including fragments thereof. Preferred binding affinities include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-6}M$ ,  $10^{-6}M$ ,  $5 \times 10^{-7}M$ ,  $10^{-7}M$ ,  $5 \times 10^{-8}M$ ,  $10^{-8}M$ ,  $5 \times 10^{-9}M$ ,  $10^{-9}M$ ,  $5 \times 10^{-10}M$ ,  $10^{-10}M$ ,  $5 \times 10^{-11}M$ ,  $10^{-11}M$ ,  $5 \times 10^{-12}M$ ,  $10^{-12}M$ ,  $5 \times 10^{-13}M$ ,  $10^{-13}M$ ,  $5 \times 10^{-14}M$ ,  $10^{-14}M$ ,  $5 \times 10^{-15}M$ , and  $10^{-15}M$ .

[0584] Moreover, ovarian antigen polypeptides of the present invention or fragments thereof, are useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere herein. In a most preferred embodiment, said anti-angiogenesis effect may be achieved indirectly, for example, through the inhibition of hematopoietic, tumor-specific cells, such as tumor-associated macrophages (see, e.g., Joseph IB, et al. J Natl Cancer Inst, 90(21):1648-53 (1998), which is hereby incorporated by reference). Antibodies directed to polypeptides or polynucleotides of the present invention may also result in inhibition of angiogenesis directly, or indirectly (see, e.g., Witte L, et al., Cancer Metastasis Rev. 17(2):155-61 (1998), which is hereby incorporated by reference)).

[0585] Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (see, e.g., Schulze-Osthoff K, et.al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will

activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuvants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, *Mutat. Res.* 400(1-2):447-55 (1998), *Med Hypotheses*.50(5):423-33 (1998), *Chem. Biol. Interact.* Apr 24;111-112:23-34 (1998), *J. Mo. Med.* 76(6):402-12 (1998), *Int. J. Tissue React.* 20(1):3-15 (1998), which are all hereby incorporated by reference).

[0586] Polypeptides, including protein fusions to, or fragments thereof, of the present invention are useful in inhibiting the metastasis of proliferative cells or tissues. Inhibition may occur as a direct result of administering polypeptides, or antibodies directed to said polypeptides as described elsewhere herein, or indirectly, such as activating the expression of proteins known to inhibit metastasis, for example alpha 4 integrins, (See, e.g., *Curr Top Microbiol Immunol* 1998;231:125-41, which is hereby incorporated by reference). Such therapeutic affects of the present invention may be achieved either alone, or in combination with small molecule drugs or adjuvants.

[0587] In another embodiment, the invention provides a method of delivering compositions containing the polypeptides of the invention (e.g., compositions containing polypeptides or anti-ovarian antigen polypeptide antibodies associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs) to targeted cells expressing the polypeptide of the present invention. Ovarian antigen polypeptides or anti- ovarian antigen polypeptide antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions.

[0588] Polypeptides, protein fusions to, or fragments thereof, of the present invention are useful in enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues, either directly, such as would occur if the polypeptides of the present invention 'vaccinated' the immune response to respond to proliferative antigens and immunogens, or indirectly, such as in activating the expression of proteins known to enhance the immune response (e.g. chemokines), to said antigens and immunogens.

### **Urinary System Disorders**

[0589] Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention, may be used to treat, prevent, diagnose, and/or prognose disorders of the urinary system, including but not limited to disorders of the renal system, bladder, ureters, and urethra. Renal disorders include, but are not limited to, kidney failure, nephritis, blood vessel disorders of kidney, metabolic and congenital kidney disorders, urinary disorders of the kidney, autoimmune disorders, sclerosis and necrosis, electrolyte imbalance, and kidney cancers.

[0590] Kidney failure diseases include, but are not limited to, acute kidney failure, chronic kidney failure, atheroembolic renal failure, and end-stage renal disease. Inflammatory diseases of the kidney include acute glomerulonephritis, postinfectious glomerulonephritis, rapidly progressive glomerulonephritis, nephrotic syndrome, membranous glomerulonephritis, familial nephrotic syndrome, membranoproliferative glomerulonephritis I and II, mesangial proliferative glomerulonephritis, chronic glomerulonephritis, acute tubulointerstitial nephritis, chronic tubulointerstitial nephritis, acute post-streptococcal glomerulonephritis (PSGN), pyelonephritis, lupus nephritis, chronic nephritis, interstitial nephritis, and post-streptococcal glomerulonephritis.

[0591] Blood vessel disorders of the kidneys include, but are not limited to, kidney infarction, atheroembolic kidney disease, cortical necrosis, malignant nephrosclerosis, renal vein thrombosis, renal underperfusion, renal ischemia-reperfusion, renal artery embolism, and renal artery stenosis. Kidney disorders resulting from urinary tract problems include, but are not limited to, pyelonephritis, hydronephrosis, urolithiasis (renal lithiasis, nephrolithiasis), reflux nephropathy, urinary tract infections, urinary retention, and acute or chronic unilateral obstructive uropathy.

[0592] Metabolic and congenital disorders of the kidneys include, but are not limited to, renal tubular acidosis, renal glycosuria, nephrogenic diabetes insipidus, cystinuria, Fanconi's syndrome, vitamin D-resistant rickets, Hartnup disease, Bartter's syndrome, Liddle's syndrome, polycystic kidney disease, medullary cystic disease, medullary sponge kidney, Alport's syndrome, nail-patella syndrome, congenital nephrotic syndrome, CRUSH syndrome, horseshoe kidney, diabetic nephropathy, nephrogenic diabetes insipidus, analgesic nephropathy, kidney stones, and membranous nephropathy. Kidney disorders resulting from an autoimmune response include, but are not limited to,

systemic lupus erythematosus (SLE), Goodpasture syndrome, IgA nephropathy, and IgM mesangial proliferative glomerulonephritis.

[0593] Sclerotic or necrotic disorders of the kidney include, but are not limited to, glomerulosclerosis, diabetic nephropathy, focal segmental glomerulosclerosis (FSGS), necrotizing glomerulonephritis, and renal papillary necrosis. Kidneys may also develop carcinomas, including, but not limited to, hypernephroma, nephroblastoma, renal cell cancer, transitional cell cancer, squamous cell cancer, and Wilm's tumor.

[0594] Kidney disorders may also result in electrolyte imbalances, including, but not limited to, nephrocalcinosis, pyuria, edema, hydronephritis, proteinuria, hyponatremia, hypernatremia, hypokalemia, hyperkalemia, hypocalcemia, hypercalcemia, hypophosphatemia, and hyperphosphatemia.

[0595] Bladder disorders include, but are not limited to, benign prostatic hyperplasia (BPH), interstitial cystitis (IC), prostatitis, proteinuria, urinary tract infections, urinary incontinence, urinary retention. Disorders of the ureters and urethra include, but are not limited to, acute or chronic unilateral obstructive uropathy. The bladder, ureters, and urethra may also develop carcinomas, including, but not limited to, superficial bladder cancer, invasive bladder cancer, carcinoma of the ureter, and urethra cancers.

[0596] Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators, gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppository solid pharmaceutical formulations, decanting or topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

### **Cardiovascular Disorders**

[0597] Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat, prevent, diagnose, and/or prognose cardiovascular disorders, including, but not limited to, peripheral artery disease, such as limb ischemia.

[0598] Cardiovascular disorders include cardiovascular abnormalities, such as arterio-arterial fistula, arteriovenous fistula, cerebral arteriovenous malformations, congenital heart defects, pulmonary atresia, and Scimitar Syndrome. Congenital heart defects include aortic coarctation, cor triatriatum, coronary vessel anomalies, crisscross heart, dextrocardia, patent ductus arteriosus, Ebstein's anomaly, Eisenmenger complex, hypoplastic left heart syndrome, levocardia, tetralogy of fallot, transposition of great vessels, double outlet right ventricle, tricuspid atresia, persistent truncus arteriosus, total anomalous pulmonary venous connection, hypoplastic left heart syndrome, and heart septal defects, such as aortopulmonary septal defect, endocardial cushion defects, Lutembacher's Syndrome, atrioventricular canal defect, trilog y of Fallot, ventricular heart septal defects.

[0599] Cardiovascular disorders also include heart disease, such as arrhythmias, carcinoid heart disease, high cardiac output, low cardiac output, cardiac tamponade, endocarditis (including bacterial), heart aneurysm, cardiac arrest, sudden cardiac death, congestive heart failure, congestive cardiomyopathy, paroxysmal dyspnea, cardiac edema, heart hypertrophy, congestive cardiomyopathy, left ventricular hypertrophy, right ventricular hypertrophy, post-infarction heart rupture, ventricular septal rupture, heart valve diseases, myocardial diseases, myocardial ischemia, pericardial effusion, pericarditis (including constrictive and tuberculous), pneumopericardium, postpericardiotomy syndrome, pulmonary heart disease, rheumatic heart disease, ventricular dysfunction, hyperemia, cardiovascular pregnancy complications, Scimitar Syndrome, diastolic dysfunction, enlarged heart, heart block, J-curve phenomenon, rheumatic heart disease, Marfan syndrome, cardiovascular syphilis, and cardiovascular tuberculosis.

[0600] Arrhythmias include sinus arrhythmia, atrial fibrillation, atrial flutter, bradycardia, extrasystole, Adams-Stokes Syndrome, bundle-branch block, sinoatrial block, long QT syndrome, parasystole, Lown-Ganong-Levine Syndrome, Mahaim-type pre-excitation syndrome, Wolff-Parkinson-White syndrome, sick sinus syndrome, tachycardias, and ventricular fibrillation. Tachycardias include paroxysmal tachycardia, supraventricular tachycardia, accelerated idioventricular rhythm, atrioventricular nodal reentry tachycardia, ectopic atrial tachycardia, ectopic junctional tachycardia, sinoatrial



nodal reentry tachycardia, sinus tachycardia, Torsades de Pointes, and ventricular tachycardia.

[0601] Heart valve disease include aortic valve insufficiency, aortic valve stenosis, heart murmurs, aortic valve prolapse, mitral valve prolapse, tricuspid valve prolapse, mitral valve insufficiency, mitral valve stenosis, pulmonary atresia, pulmonary valve insufficiency, pulmonary valve stenosis, tricuspid atresia, tricuspid valve insufficiency, tricuspid valve stenosis, and bicuspid aortic valve.

[0602] Myocardial diseases include alcoholic cardiomyopathy, congestive cardiomyopathy, hypertrophic cardiomyopathy, aortic subvalvular stenosis, pulmonary subvalvular stenosis, restrictive cardiomyopathy, Chagas cardiomyopathy, endocardial fibroelastosis, endomyocardial fibrosis, Kearns Syndrome, Barth syndrome, myocardial reperfusion injury, and myocarditis.

[0603] Myocardial ischemias include coronary disease, such as angina pectoris, Prinzmetal's angina, unstable angina, coronary aneurysm, coronary arteriosclerosis, coronary thrombosis, coronary vasospasm, myocardial infarction and myocardial stunning.

[0604] Cardiovascular diseases also include vascular diseases such as aneurysms, angiodyplasia, angiomatosis, bacillary angiomatosis, Hippel-Lindau Disease, Klippel-Trenaunay-Weber Syndrome, Sturge-Weber Syndrome, angioneurotic edema, aortic diseases, Takayasu's Arteritis, aortitis, Leriche's Syndrome, arterial occlusive diseases, arteritis, enarteritis, polyarteritis nodosa, cerebrovascular disorders, diabetic angiopathies, diabetic retinopathy, embolisms, thrombosis, erythromelalgia, hemorrhoids, hepatic veno-occlusive disease, hypertension, hypotension (shock), ischemia, peripheral vascular diseases, phlebitis, superficial phlebitis, pulmonary veno-occlusive disease, chronic obstructive pulmonary disease, Buerger's disease, Raynaud's disease, CREST syndrome, retinal vein occlusion, Scimitar syndrome, superior vena cava syndrome, telangiectasia, atacia telangiectasia, hereditary hemorrhagic telangiectasia, deep vein thrombosis, varicocele, varicose veins, varicose ulcer, vasculitis, and venous insufficiency.

[0605] Aneurysms include dissecting aneurysms, false aneurysms, infected aneurysms, ruptured aneurysms, aortic aneurysms, cerebral aneurysms, coronary aneurysms, heart aneurysms, and iliac aneurysms.

[0606] Arterial occlusive diseases include arteriosclerosis, arteriolosclerosis, atherosclerosis, intermittent claudication, carotid stenosis, fibromuscular dysplasias, mesenteric vascular occlusion, Moyamoya disease, renal artery obstruction, retinal artery occlusion, and thromboangiitis obliterans.

[0607] Cerebrovascular disorders include carotid artery diseases, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformation, cerebral artery diseases, cerebral embolism and thrombosis, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, cerebral hemorrhage, epidural hematoma, subdural hematoma, subarachnoid hemorrhage, cerebral infarction, cerebral ischemia (including transient), subclavian steal syndrome, periventricular leukomalacia, vascular headache, cluster headache, migraine, and vertebrobasilar insufficiency.

[0608] Embolisms include air embolisms, amniotic fluid embolisms, cholesterol embolisms, blue toe syndrome, fat embolisms, pulmonary embolisms, and thromboembolisms. Thrombosis include coronary thrombosis, hepatic vein thrombosis, deep vein thrombosis, retinal vein occlusion, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, and thrombophlebitis.

[0609] Ischemia includes cerebral ischemia, ischemic colitis, silent ischemia, compartment syndromes, anterior compartment syndrome, myocardial ischemia, reperfusion injuries, and peripheral limb ischemia. Vasculitis includes aortitis, arteritis, Behcet's Syndrome, Churg-Strauss Syndrome, mucocutaneous lymph node syndrome, thromboangiitis obliterans, hypersensitivity vasculitis, Schoenlein-Henoch purpura, allergic cutaneous vasculitis, and Wegener's granulomatosis.

[0610] Cardiovascular diseases can also occur due to electrolyte imbalances that include, but are not limited to hyponatremia, hypernatremia, hypokalemia, hyperkalemia, hypocalcemia, hypercalcemia, hypophosphatemia, and hyperphosphatemia. Neoplasm and/or cancers of the cardiovascular system include, but are not limited to, myxomas, fibromas, and rhabdomyomas.

[0611] Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators,

gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppositorial solid pharmaceutical formulations, decanting or topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

### **Respiratory Disorders**

[0612] Polynucleotides or polypeptides, or agonists or antagonists of the present invention may be used to treat, prevent, diagnose, and/or prognose diseases and/or disorders of the respiratory system.

[0613] Diseases and disorders of the respiratory system include, but are not limited to, nasal vestibulitis, nonallergic rhinitis (e.g., acute rhinitis, chronic rhinitis, atrophic rhinitis, vasomotor rhinitis), nasal polyps, and sinusitis, juvenile angiofibromas, cancer of the nose and juvenile papillomas, vocal cord polyps, nodules (singer's nodules), contact ulcers, vocal cord paralysis, laryngoceles, pharyngitis (e.g., viral and bacterial), tonsillitis, tonsillar cellulitis, parapharyngeal abscess, laryngitis, laryngoceles, and throat cancers (e.g., cancer of the nasopharynx, tonsil cancer, larynx cancer), lung cancer (e.g., squamous cell carcinoma, small cell (oat cell) carcinoma, large cell carcinoma, and adenocarcinoma), allergic disorders (eosinophilic pneumonia, hypersensitivity pneumonitis (e.g., extrinsic allergic alveolitis, allergic interstitial pneumonitis, organic dust pneumoconiosis, allergic bronchopulmonary aspergillosis, asthma, Wegener's granulomatosis (granulomatous vasculitis), Goodpasture's syndrome)), pneumonia (e.g., bacterial pneumonia (e.g., *Streptococcus pneumoniae* (pneumococcal pneumonia), *Staphylococcus aureus* (staphylococcal pneumonia), Gram-negative bacterial pneumonia (caused by, e.g., *Klebsiella* and *Pseudomonas spp.*), *Mycoplasma pneumoniae* pneumonia, *Hemophilus influenzae* pneumonia, *Legionella pneumophila* (Legionnaires' disease), and *Chlamydia psittaci* (Psittacosis)), and viral pneumonia (e.g., influenza, chickenpox (varicella).

[0614] Additional diseases and disorders of the respiratory system include, but are not limited to bronchiolitis, polio (poliomyelitis), croup, respiratory syncytial viral infection, mumps, erythema infectiosum (fifth disease), roseola infantum, progressive

rubella panencephalitis, german measles, and subacute sclerosing panencephalitis), fungal pneumonia (e.g., Histoplasmosis, Coccidioidomycosis, Blastomycosis, fungal infections in people with severely suppressed immune systems (e.g., cryptococcosis, caused by *Cryptococcus neoformans*; aspergillosis, caused by *Aspergillus spp.*; candidiasis, caused by *Candida*; and mucormycosis)), *Pneumocystis carinii* (pneumocystis pneumonia), atypical pneumonias (e.g., *Mycoplasma* and *Chlamydia spp.*), opportunistic infection pneumonia, nosocomial pneumonia, chemical pneumonitis, and aspiration pneumonia, pleural disorders (e.g., pleurisy, pleural effusion, and pneumothorax (e.g., simple spontaneous pneumothorax, complicated spontaneous pneumothorax, tension pneumothorax)), obstructive airway diseases (e.g., asthma, chronic obstructive pulmonary disease (COPD), emphysema, chronic or acute bronchitis), occupational lung diseases (e.g., silicosis, black lung (coal workers' pneumoconiosis), asbestosis, berylliosis, occupational asthma, byssinosis, and benign pneumoconioses), Infiltrative Lung Disease (e.g., pulmonary fibrosis (e.g., fibrosing alveolitis, usual interstitial pneumonia), idiopathic pulmonary fibrosis, desquamative interstitial pneumonia, lymphoid interstitial pneumonia, histiocytosis X (e.g., Letterer-Siwe disease, Hand-Schüller-Christian disease, eosinophilic granuloma), idiopathic pulmonary hemosiderosis, sarcoidosis and pulmonary alveolar proteinosis), Acute respiratory distress syndrome (also called, e.g., adult respiratory distress syndrome), edema, pulmonary embolism, bronchitis (e.g., viral, bacterial), bronchiectasis, atelectasis, lung abscess (caused by, e.g., *Staphylococcus aureus* or *Legionella pneumophila*), and cystic fibrosis.

#### Anti-Angiogenesis Activity

[0615] The naturally occurring balance between endogenous stimulators and inhibitors of angiogenesis is one in which inhibitory influences predominate. Rastinejad *et al.*, *Cell* 56:345-355 (1989). In those rare instances in which neovascularization occurs under normal physiological conditions, such as wound healing, organ regeneration, embryonic development, and female reproductive processes, angiogenesis is stringently regulated and spatially and temporally delimited. Under conditions of pathological angiogenesis such as that characterizing solid tumor growth, these regulatory controls fail. Unregulated angiogenesis becomes pathologic and sustains progression of many

neoplastic and non-neoplastic diseases. A number of serious diseases are dominated by abnormal neovascularization including solid tumor growth and metastases, arthritis, some types of eye disorders, and psoriasis. See, e.g., reviews by Moses *et al.*, *Biotech.* 9:630-634 (1991); Folkman *et al.*, *N. Engl. J. Med.*, 333:1757-1763 (1995); Auerbach *et al.*, *J. Microvasc. Res.* 29:401-411 (1985); Folkman, *Advances in Cancer Research*, eds. Klein and Weinhouse, Academic Press, New York, pp. 175-203 (1985); Patz, *Am. J. Ophthalmol.* 94:715-743 (1982); and Folkman *et al.*, *Science* 221:719-725 (1983). In a number of pathological conditions, the process of angiogenesis contributes to the disease state. For example, significant data have accumulated which suggest that the growth of solid tumors is dependent on angiogenesis. Folkman and Klagsbrun, *Science* 235:442-447 (1987).

[0616] The present invention provides for treatment of diseases or disorders associated with neovascularization by administration of the polynucleotides and/or polypeptides of the invention, as well as agonists or antagonists of the present invention. Malignant and metastatic conditions which can be treated with the polynucleotides and polypeptides, or agonists or antagonists of the invention include, but are not limited to, malignancies, solid tumors, and cancers described herein and otherwise known in the art (for a review of such disorders, see Fishman *et al.*, *Medicine*, 2d Ed., J. B. Lippincott Co., Philadelphia (1985)). Thus, the present invention provides a method of treating an angiogenesis-related disease and/or disorder, comprising administration to an individual in need thereof a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist of the invention. For example, polynucleotides, polypeptides, antagonists and/or agonists may be utilized in a variety of additional methods in order to therapeutically treat a cancer or tumor. Cancers which may be treated with polynucleotides, polypeptides, antagonists and/or agonists include, but are not limited to solid tumors, including prostate, lung, breast, ovarian, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer; primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non-small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias. For example, polynucleotides, polypeptides, antagonists and/or agonists may be delivered topically, in order to treat cancers such as skin cancer, head and neck tumors, breast tumors, and

Kaposi's sarcoma.

[0617] Within yet other aspects, polynucleotides, polypeptides, antagonists and/or agonists may be utilized to treat superficial forms of bladder cancer by, for example, intravesical administration. Polynucleotides, polypeptides, antagonists and/or agonists may be delivered directly into the tumor, or near the tumor site, via injection or a catheter. Of course, as the artisan of ordinary skill will appreciate, the appropriate mode of administration will vary according to the cancer to be treated. Other modes of delivery are discussed herein.

[0618] Polynucleotides, polypeptides, antagonists and/or agonists may be useful in treating other disorders, besides cancers, which involve angiogenesis. These disorders include, but are not limited to: benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophilic joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis.

[0619] For example, within one aspect of the present invention methods are provided for treating hypertrophic scars and keloids, comprising the step of administering a polynucleotide, polypeptide, antagonist and/or agonist of the invention to a hypertrophic scar or keloid.

[0620] Within one embodiment of the present invention polynucleotides, polypeptides, antagonists and/or agonists of the invention are directly injected into a hypertrophic scar or keloid, in order to prevent the progression of these lesions. This therapy is of particular value in the prophylactic treatment of conditions which are known to result in the development of hypertrophic scars and keloids (e.g., burns), and is

preferably initiated after the proliferative phase has had time to progress (approximately 14 days after the initial injury), but before hypertrophic scar or keloid development. As noted above, the present invention also provides methods for treating neovascular diseases of the eye, including for example, corneal neovascularization, neovascular glaucoma, proliferative diabetic retinopathy, retrolental fibroplasia and macular degeneration.

[0621] Moreover, ocular disorders associated with neovascularization which can be treated with the polynucleotides and polypeptides of the present invention (including agonists and/or antagonists) include, but are not limited to: neovascular glaucoma, diabetic retinopathy, retinoblastoma, retrolental fibroplasia, uveitis, retinopathy of prematurity, macular degeneration, corneal graft neovascularization, as well as other eye inflammatory diseases, ocular tumors and diseases associated with choroidal or iris neovascularization. See, e.g., reviews by Waltman *et al.*, *Am. J. Ophthalmol.* 85:704-710 (1978) and Gartner *et al.*, *Surv. Ophthalmol.* 22:291-312 (1978).

[0622] Thus, within one aspect of the present invention methods are provided for treating neovascular diseases of the eye such as corneal neovascularization (including corneal graft neovascularization), comprising the step of administering to a patient a therapeutically effective amount of a compound (as described above) to the cornea, such that the formation of blood vessels is inhibited. Briefly, the cornea is a tissue, which normally lacks blood vessels. In certain pathological conditions however, capillaries may extend into the cornea from the pericorneal vascular plexus of the limbus. When the cornea becomes vascularized, it also becomes clouded, resulting in a decline in the patient's visual acuity. Visual loss may become complete if the cornea completely opacitates. A wide variety of disorders can result in corneal neovascularization, including for example, corneal infections (e.g., trachoma, herpes simplex keratitis, leishmaniasis and onchocerciasis), immunological processes (e.g., graft rejection and Stevens-Johnson's syndrome), alkali burns, trauma, inflammation (of any cause), toxic and nutritional deficiency states, and as a complication of wearing contact lenses.

[0623] Within particularly preferred embodiments of the invention, may be prepared for topical administration in saline (combined with any of the preservatives and antimicrobial agents commonly used in ocular preparations), and administered in eyedrop form. The solution or suspension may be prepared in its pure form and administered

several times daily. Alternatively, anti-angiogenic compositions, prepared as described above, may also be administered directly to the cornea. Within preferred embodiments, the anti-angiogenic composition is prepared with a muco-adhesive polymer, which binds to cornea. Within further embodiments, the anti-angiogenic factors or anti-angiogenic compositions may be utilized as an adjunct to conventional steroid therapy. Topical therapy may also be useful prophylactically in corneal lesions which are known to have a high probability of inducing an angiogenic response (such as chemical burns). In these instances the treatment, likely in combination with steroids, may be instituted immediately to help prevent subsequent complications.

[0624] Within other embodiments, the compounds described above may be injected directly into the corneal stroma by an ophthalmologist under microscopic guidance. The preferred site of injection may vary with the morphology of the individual lesion, but the goal of the administration would be to place the composition at the advancing front of the vasculature (i.e., interspersed between the blood vessels and the normal cornea). In most cases this would involve perilimbic corneal injection to "protect" the cornea from the advancing blood vessels. This method may also be utilized shortly after a corneal insult in order to prophylactically prevent corneal neovascularization. In this situation, the material could be injected in the perilimbic cornea interspersed between the corneal lesion and its undesired potential limbic blood supply. Such methods may also be utilized in a similar fashion to prevent capillary invasion of transplanted corneas. In a sustained-release form, injections might only be required 2-3 times per year. A steroid could also be added to the injection solution to reduce inflammation resulting from the injection itself.

[0625] Within another aspect of the present invention, methods are provided for treating neovascular glaucoma, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. In one embodiment, the compound may be administered topically to the eye in order to treat early forms of neovascular glaucoma. Within other embodiments, the compound may be implanted by injection into the region of the anterior chamber angle. Within other embodiments, the compound may also be placed in any location such that the compound is



continuously released into the aqueous humor. Within another aspect of the present invention, methods are provided for treating proliferative diabetic retinopathy, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eyes, such that the formation of blood vessels is inhibited.

[0626] Within particularly preferred embodiments of the invention, proliferative diabetic retinopathy may be treated by injection into the aqueous humor or the vitreous, in order to increase the local concentration of the polynucleotide, polypeptide, antagonist and/or agonist in the retina. Preferably, this treatment should be initiated prior to the acquisition of severe disease requiring photocoagulation.

[0627] Within another aspect of the present invention, methods are provided for treating retrolental fibroplasia, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. The compound may be administered topically, via intravitreal injection and/or via intraocular implants.

[0628] Additionally, disorders which can be treated with the polynucleotides, polypeptides, agonists and/or antagonists include, but are not limited to, hemangioma, arthritis, psoriasis, angiofibroma, atherosclerotic plaques, delayed wound healing, granulations, hemophilic joints, hypertrophic scars, nonunion fractures, Osler-Weber syndrome, pyogenic granuloma, scleroderma, trachoma, and vascular adhesions.

[0629] Moreover, disorders and/or states, which can be treated, prevented, diagnosed and/or prognosed with the polynucleotides, polypeptides, agonists and/or antagonists of the invention include, but are not limited to, solid tumors, blood born tumors such as leukemias, tumor metastasis, Kaposi's sarcoma, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas, rheumatoid arthritis, psoriasis, ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, and uveitis, delayed wound healing, endometriosis, vasculogenesis, granulations, hypertrophic scars (keloids), nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations,

ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma fibromuscular dysplasia, wound granulation, Crohn's disease, atherosclerosis, birth control agent by preventing vascularization required for embryo implantation controlling menstruation, diseases that have angiogenesis as a pathologic consequence such as cat scratch disease (*Rochelina quintosa*), ulcers (*Helicobacter pylori*), Bartonellosis and bacillary angiomatosis.

[0630] In one aspect of the birth control method, an amount of the compound sufficient to block embryo implantation is administered before or after intercourse and fertilization have occurred, thus providing an effective method of birth control, possibly a "morning after" method. Polynucleotides, polypeptides, agonists and/or antagonists may also be used in controlling menstruation or administered as either a peritoneal lavage fluid or for peritoneal implantation in the treatment of endometriosis.

[0631] Polynucleotides, polypeptides, agonists and/or antagonists of the present invention may be incorporated into surgical sutures in order to prevent stitch granulomas.

[0632] Polynucleotides, polypeptides, agonists and/or antagonists may be utilized in a wide variety of surgical procedures. For example, within one aspect of the present invention a composition (in the form of, for example, a spray or film) may be utilized to coat or spray an area prior to removal of a tumor, in order to isolate normal surrounding tissues from malignant tissue, and/or to prevent the spread of disease to surrounding tissues. Within other aspects of the present invention, compositions (e.g., in the form of a spray) may be delivered via endoscopic procedures in order to coat tumors, or inhibit angiogenesis in a desired locale. Within yet other aspects of the present invention, surgical meshes, which have been coated with anti-angiogenic compositions of the present invention may be utilized in any procedure wherein a surgical mesh might be utilized. For example, within one embodiment of the invention a surgical mesh laden with an anti-angiogenic composition may be utilized during abdominal cancer resection surgery (e.g., subsequent to colon resection) in order to provide support to the structure, and to release an amount of the anti-angiogenic factor.

[0633] Within further aspects of the present invention, methods are provided for treating tumor excision sites, comprising administering a polynucleotide, polypeptide, agonist and/or antagonist to the resection margins of a tumor subsequent to excision, such

that the local recurrence of cancer and the formation of new blood vessels at the site is inhibited. Within one embodiment of the invention, the anti-angiogenic compound is administered directly to the tumor excision site (e.g., applied by swabbing, brushing or otherwise coating the resection margins of the tumor with the anti-angiogenic compound). Alternatively, the anti-angiogenic compounds may be incorporated into known surgical pastes prior to administration. Within particularly preferred embodiments of the invention, the anti-angiogenic compounds are applied after hepatic resections for malignancy, and after neurosurgical operations.

[0634] Within one aspect of the present invention, polynucleotides, polypeptides, agonists and/or antagonists may be administered to the resection margin of a wide variety of tumors, including for example, breast, colon, brain and hepatic tumors. For example, within one embodiment of the invention, anti-angiogenic compounds may be administered to the site of a neurological tumor subsequent to excision, such that the formation of new blood vessels at the site are inhibited.

[0635] The polynucleotides, polypeptides, agonists and/or antagonists of the present invention may also be administered along with other anti-angiogenic factors. Representative examples of other anti-angiogenic factors include: Anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel, Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

[0636] Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

[0637] Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

[0638] Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

[0639] A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells), (Murata et al., Cancer Res. 51:22-26 (1991)); Sulphated Polysaccharide Peptidoglycan Complex (SP- PG) (the function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cishydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin; Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio. Chem. 267:17321-17326 (1992)); Chymostatin (Tomkinson et al., Biochem J. 286:475-480 (1992)); Cyclodextrin Tetradecasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557 (1990)); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446 (1987)); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664 (1987)); Bisantrene (National Cancer Institute); Lobenzarit disodium (N-(2)-carboxyphenyl-4- chloroanthronilic acid disodium or "CCA"; Takeuchi et al., Agents Actions 36:312-316, 1992); Thalidomide; Angostatic steroid; AGM-1470; carboxyaminolimidazole; and metalloproteinase inhibitors such as BB94.

### **Musculoskeletal System Disorders**

[0640] Polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention, may be used to treat, prevent, diagnose, and/or prognose disorders of the musculoskeletal system, including but not limited to, disorders of the bone, joints, ligaments, tendons, bursa, muscle, and/or neoplasms and cancers associated with musculoskeletal tissue.

[0641] Diseases or disorders of the bone include, but are not limited to, Albers-Schönberg disease, bowlegs, heel spurs, Köhler's bone disease, knock-knees, Legg-Calvé-Perthes disease, Marfan's syndrome, mucopolysaccharidoses, Osgood-Schlatter disease, osteochondroses, osteochondrodysplasia, osteomyelitis, osteopetroses, osteoporosis (postmenopausal, senile, and juvenile), Paget's disease, Scheuermann's disease, scoliosis, Sever's disease, and patellofemoral stress syndrome.

[0642] Joint diseases or disorders include, but are not limited to, ankylosing spondylitis, Behçet's syndrome, CREST syndrome, Ehlers-Danlos syndrome, infectious arthritis, discoid lupus erythematosus, systemic lupus erythematosus, Lyme disease, osteoarthritis, psoriatic arthritis, relapsing polychondrites, Reiter's syndrome, rheumatoid arthritis (adult and juvenile), scleroderma, and Still's disease.

[0643] Diseases or disorders affecting ligaments, tendons, or bursa include, but are not limited to, ankle sprain, bursitis, posterior Achilles tendon bursitis (Haglund's deformity), anterior Achilles tendon bursitis (Albert's disease), tendinitis, tenosynovitis, popliteus tendinitis, Achilles tendinitis, medial or lateral epicondylitis, rotator cuff tendinitis, spasmodic torticollis, and fibromyalgia syndrome.

[0644] Muscle diseases or disorders include, but are not limited to, Becker's muscular dystrophy, Duchenne's muscular dystrophy, Landouzy-Dejerine muscular dystrophy, Leyden-Möbius muscular dystrophy, Erb's muscular dystrophy, Charcot's joints, dermatomyositis, gout, pseudogout, glycogen storage diseases, Pompe's disease, mitochondrial myopathy, periodic paralysis, polymyalgia rheumatica, polymyositis, Steinert's disease, Thomsen's disease, anterolateral and posteromedial shin splints, posterior femoral muscle strain, and fibromyositis.

[0645] Musculoskeletal tissue may also develop cancers and/or neoplasms that include, but are not limited to, osteochondroma, benign chondroma, chondroblastoma,

chondromyxoid fibroma, osteoid osteoma, giant cell tumor, multiple myeloma, osteosarcoma, fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's tumor, and malignant lymphoma of bone.

### **Neural Activity and Neurological Diseases**

[0646] The polynucleotides, polypeptides and agonists or antagonists of the invention may be used for the diagnosis and/or treatment of diseases, disorders, damage or injury of the brain and/or nervous system. Nervous system disorders that can be treated with the compositions of the invention (e.g., polypeptides, polynucleotides, and/or agonists or antagonists), include, but are not limited to, nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the methods of the invention, include but are not limited to, the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems: (1) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia; (2) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions which sever a portion of the nervous system, or compression injuries; (3) malignant lesions, in which a portion of the nervous system is destroyed or injured by malignant tissue which is either a nervous system associated malignancy or a malignancy derived from non-nervous system tissue; (4) infectious lesions, in which a portion of the nervous system is destroyed or injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, or syphilis; (5) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to, degeneration associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis (ALS); (6) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including, but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke

disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis; (8) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and (9) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including, but not limited to, multiple sclerosis, human immunodeficiency virus-associated myelopathy, transverse myelopathy or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

[0647] In one embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to protect neural cells from the damaging effects of hypoxia. In a further preferred embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to protect neural cells from the damaging effects of cerebral hypoxia. According to this embodiment, the compositions of the invention are used to treat or prevent neural cell injury associated with cerebral hypoxia. In one non-exclusive aspect of this embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention, are used to treat or prevent neural cell injury associated with cerebral ischemia. In another non-exclusive aspect of this embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to treat or prevent neural cell injury associated with cerebral infarction.

[0648] In another preferred embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to treat or prevent neural cell injury associated with a stroke. In a specific embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to treat or prevent cerebral neural cell injury associated with a stroke.

[0649] In another preferred embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to treat or prevent neural cell injury associated with a heart attack. In a specific embodiment, the polypeptides, polynucleotides, or agonists or antagonists of the invention are used to treat or prevent cerebral neural cell injury associated with a heart attack.

[0650] The compositions of the invention which are useful for treating or preventing a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, compositions of the invention which elicit any of the following effects may be useful according to the invention: (1) increased survival time of neurons in culture either in the presence or absence of hypoxia or hypoxic conditions; (2) increased sprouting of neurons in culture or *in vivo*; (3) increased production of a neuron-associated molecule in culture or *in vivo*, e.g., choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or (4) decreased symptoms of neuron dysfunction *in vivo*. Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may routinely be measured using a method set forth herein or otherwise known in the art, such as, for example, in Zhang *et al.*, *Proc Natl Acad Sci USA* 97:3637-42 (2000) or in Arakawa *et al.*, *J. Neurosci.*, 10:3507-15 (1990); increased sprouting of neurons may be detected by methods known in the art, such as, for example, the methods set forth in Pestronk *et al.*, *Exp. Neurol.*, 70:65-82 (1980), or Brown *et al.*, *Ann. Rev. Neurosci.*, 4:17-42 (1981); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, etc., using techniques known in the art and depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, e.g., weakness, motor neuron conduction velocity, or functional disability.

[0651] In specific embodiments, motor neuron disorders that may be treated according to the invention include, but are not limited to, disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including, but not limited to, progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).



[0652] Further, polypeptides or polynucleotides of the invention may play a role in neuronal survival; synapse formation; conductance; neural differentiation, etc. Thus, compositions of the invention (including polynucleotides, polypeptides, and agonists or antagonists) may be used to diagnose and/or treat or prevent diseases or disorders associated with these roles, including, but not limited to, learning and/or cognition disorders. The compositions of the invention may also be useful in the treatment or prevention of neurodegenerative disease states and/or behavioural disorders. Such neurodegenerative disease states and/or behavioral disorders include, but are not limited to, Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, compositions of the invention may also play a role in the treatment, prevention and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders.

[0653] Additionally, polypeptides, polynucleotides and/or agonists or antagonists of the invention, may be useful in protecting neural cells from diseases, damage, disorders, or injury, associated with cerebrovascular disorders including, but not limited to, carotid artery diseases (e.g., carotid artery thrombosis, carotid stenosis, or Moyamoya Disease), cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformations, cerebral artery diseases, cerebral embolism and thrombosis (e.g., carotid artery thrombosis, sinus thrombosis, or Wallenberg's Syndrome), cerebral hemorrhage (e.g., epidural or subdural hematoma, or subarachnoid hemorrhage), cerebral infarction, cerebral ischemia (e.g., transient cerebral ischemia, Subclavian Steal Syndrome, or vertebrobasilar insufficiency), vascular dementia (e.g., multi-infarct), leukomalacia, periventricular, and vascular headache (e.g., cluster headache or migraines).

[0654] In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate neurological cell proliferation and/or differentiation. Therefore, polynucleotides, polypeptides, agonists and/or antagonists of the invention may be used to treat and/or detect neurologic diseases. Moreover, polynucleotides or polypeptides, or agonists or

antagonists of the invention, can be used as a marker or detector of a particular nervous system disease or disorder.

[0655] Examples of neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include brain diseases, such as metabolic brain diseases which includes phenylketonuria such as maternal phenylketonuria; pyruvate carboxylase deficiency, pyruvate dehydrogenase complex deficiency, Wernicke's Encephalopathy, brain edema, brain neoplasms such as cerebellar neoplasms which include infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms, supratentorial neoplasms, canavan disease, cerebellar diseases such as cerebellar ataxia which include spinocerebellar degeneration such as ataxia telangiectasia, cerebellar dyssynergia, Friederich's Ataxia, Machado-Joseph Disease, olivopontocerebellar atrophy, cerebellar neoplasms such as infratentorial neoplasms, diffuse cerebral sclerosis such as encephalitis periaxialis, globoid cell leukodystrophy, metachromatic leukodystrophy and subacute sclerosing panencephalitis.

[0656] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include cerebrovascular disorders (such as carotid artery diseases which include carotid artery thrombosis, carotid stenosis and Moyamoya Disease), cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformations, cerebral artery diseases, cerebral embolism and thrombosis such as carotid artery thrombosis, sinus thrombosis and Wallenberg's Syndrome, cerebral hemorrhage such as epidural hematoma, subdural hematoma and subarachnoid hemorrhage, cerebral infarction, cerebral ischemia such as transient cerebral ischemia, Subclavian Steal Syndrome and vertebrobasilar insufficiency, vascular dementia such as multi-infarct dementia, periventricular leukomalacia, vascular headache such as cluster headache and migraine.

[0657] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include dementia such as AIDS Dementia Complex, presenile dementia such as Alzheimer's Disease and Creutzfeldt-Jakob Syndrome, senile dementia such as

Alzheimer's Disease and progressive supranuclear palsy, vascular dementia such as multi-infarct dementia, encephalitis which include encephalitis periaxialis, viral encephalitis such as epidemic encephalitis, Japanese Encephalitis, St. Louis Encephalitis, tick-borne encephalitis and West Nile Fever, acute disseminated encephalomyelitis, meningoencephalitis such as uveomeningoencephalitic syndrome, Postencephalitic Parkinson Disease and subacute sclerosing panencephalitis, encephalomalacia such as periventricular leukomalacia, epilepsy such as generalized epilepsy which includes infantile spasms, absence epilepsy, myoclonic epilepsy which includes MERRF Syndrome, tonic-clonic epilepsy, partial epilepsy such as complex partial epilepsy, frontal lobe epilepsy and temporal lobe epilepsy, post-traumatic epilepsy, status epilepticus such as Epilepsia Partialis Continua, and Hallervorden-Spatz Syndrome.

[0658] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides; agonists, and/or antagonists of the present invention include hydrocephalus such as Dandy-Walker Syndrome and normal pressure hydrocephalus, hypothalamic diseases such as hypothalamic neoplasms, cerebral malaria, narcolepsy which includes cataplexy, bulbar poliomyelitis, cerebri pseudotumor, Rett Syndrome, Reye's Syndrome, thalamic diseases, cerebral toxoplasmosis, intracranial tuberculoma and Zellweger Syndrome, central nervous system infections such as AIDS Dementia Complex, Brain Abscess, subdural empyema, encephalomyelitis such as Equine Encephalomyelitis, Venezuelan Equine Encephalomyelitis, Necrotizing Hemorrhagic Encephalomyelitis, Visna, and cerebral malaria.

[0659] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include meningitis such as arachnoiditis, aseptic meningitis such as viral meningitis which includes lymphocytic choriomeningitis, Bacterial meningitis which includes Haemophilus Meningitis, Listeria Meningitis, Meningococcal Meningitis such as Waterhouse-Friderichsen Syndrome, Pneumococcal Meningitis and meningeal tuberculosis, fungal meningitis such as Cryptococcal Meningitis, subdural effusion, meningoencephalitis such as uveomeningoencephalitic syndrome, myelitis such as transverse myelitis, neurosyphilis such as tabes dorsalis, poliomyelitis which includes bulbar poliomyelitis and postpoliomyelitis syndrome, prion diseases (such as Creutzfeldt-

Jakob Syndrome, Bovine Spongiform Encephalopathy, Gerstmann-Straussler Syndrome, Kuru, Scrapie), and cerebral toxoplasmosis.

[0660] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include central nervous system neoplasms such as brain neoplasms that include cerebellar neoplasms such as infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms and supratentorial neoplasms, meningeal neoplasms, spinal cord neoplasms which include epidural neoplasms, demyelinating diseases such as Canavan Diseases, diffuse cerebral sclerosis which includes adrenoleukodystrophy, encephalitis periaxialis, globoid cell leukodystrophy, diffuse cerebral sclerosis such as metachromatic leukodystrophy, allergic encephalomyelitis, necrotizing hemorrhagic encephalomyelitis, progressive multifocal leukoencephalopathy, multiple sclerosis, central pontine myelinolysis, transverse myelitis, neuromyelitis optica, Scrapie, Swayback, Chronic Fatigue Syndrome, Visna, High Pressure Nervous Syndrome, Meningism, spinal cord diseases such as amyotonia congenita, amyotrophic lateral sclerosis, spinal muscular atrophy such as Werdnig-Hoffmann Disease, spinal cord compression, spinal cord neoplasms such as epidural neoplasms, syringomyelia, Tabes Dorsalis, Stiff-Man Syndrome, mental retardation such as Angelman Syndrome, Cri-du-Chat Syndrome, De Lange's Syndrome, Down Syndrome, Gangliosidoses such as gangliosidoses G(M1), Sandhoff Disease, Tay-Sachs Disease, Hartnup Disease, homocystinuria, Laurence-Moon- Biedl Syndrome, Lesch-Nyhan Syndrome, Maple Syrup Urine Disease, mucopolysaccharidosis such as fucosidosis, neuronal ceroid-lipofuscinosis, oculocerebrorenal syndrome, phenylketonuria such as maternal phenylketonuria, Prader-Willi Syndrome, Rett Syndrome, Rubinstein-Taybi Syndrome, Tuberous Sclerosis, WAGR Syndrome, nervous system abnormalities such as holoprosencephaly, neural tube defects such as anencephaly which includes hydranencephaly, Arnold-Chiari Deformity, encephalocele, meningocele, meningomyelocele, spinal dysraphism such as spina bifida cystica and spina bifida occulta.

[0661] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include hereditary motor and sensory neuropathies which include Charcot-Marie Disease,

Hereditary optic atrophy, Refsum's Disease, hereditary spastic paraplegia, Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies such as Congenital Analgesia and Familial Dysautonomia, Neurologic manifestations (such as agnosia that include Gerstmann's Syndrome, Amnesia such as retrograde amnesia, apraxia, neurogenic bladder, cataplexy, communicative disorders such as hearing disorders that includes deafness, partial hearing loss, loudness recruitment and tinnitus, language disorders such as aphasia which include agraphia, anomia, broca aphasia, and Wernicke Aphasia, Dyslexia such as Acquired Dyslexia, language development disorders, speech disorders such as aphasia which includes anomia, broca aphasia and Wernicke Aphasia, articulation disorders, communicative disorders such as speech disorders which include dysarthria, echolalia, mutism and stuttering, voice disorders such as aphonia and hoarseness, decerebrate state, delirium, fasciculation, hallucinations, meningism, movement disorders such as angelman syndrome, ataxia, athetosis, chorea, dystonia, hypokinesia, muscle hypotonia, myoclonus, tic, torticollis and tremor, muscle hypertonia such as muscle rigidity such as stiff-man syndrome, muscle spasticity, paralysis such as facial paralysis which includes Herpes Zoster Oticus, Gastroparesis, Hemiplegia, ophthalmoplegia such as diplopia, Duane's Syndrome, Horner's Syndrome, Chronic progressive external ophthalmoplegia such as Kearns Syndrome, Bulbar Paralysis, Tropical Spastic Paraparesis, Paraplegia such as Brown-Sequard Syndrome, quadriplegia, respiratory paralysis and vocal cord paralysis, paresis, phantom limb, taste disorders such as ageusia and dysgeusia, vision disorders such as amblyopia, blindness, color vision defects, diplopia, hemianopsia, scotoma and subnormal vision, sleep disorders such as hypersomnia which includes Kleine-Levin Syndrome, insomnia, and somnambulism, spasm such as trismus, unconsciousness such as coma, persistent vegetative state and syncope and vertigo, neuromuscular diseases such as amyotonia congenita, amyotrophic lateral sclerosis, Lambert-Eaton Myasthenic Syndrome, motor neuron disease, muscular atrophy such as spinal muscular atrophy, Charcot-Marie Disease and Werdnig-Hoffmann Disease, Postpoliomyelitis Syndrome, Muscular Dystrophy, Myasthenia Gravis, Myotonia Atrophica, Myotonia Confenita, Nemaline Myopathy, Familial Periodic Paralysis, Multiplex Paramyoclonus, Tropical Spastic Paraparesis and Stiff-Man Syndrome, peripheral nervous system diseases such as acrodynia, amyloid neuropathies, autonomic

nervous system diseases such as Adie's Syndrome, Barre-Lieou Syndrome, Familial Dysautonomia, Horner's Syndrome, Reflex Sympathetic Dystrophy and Shy-Drager Syndrome, Cranial Nerve Diseases such as Acoustic Nerve Diseases such as Acoustic Neuroma which includes Neurofibromatosis 2, Facial Nerve Diseases such as Facial Neuralgia, Melkersson-Rosenthal Syndrome, ocular motility disorders which includes amblyopia, nystagmus, oculomotor nerve paralysis, ophthalmoplegia such as Duane's Syndrome, Horner's Syndrome, Chronic Progressive External Ophthalmoplegia which includes Kearns Syndrome, Strabismus such as Esotropia and Exotropia, Oculomotor Nerve Paralysis, Optic Nerve Diseases such as Optic Atrophy which includes Hereditary Optic Atrophy, Optic Disk Drusen, Optic Neuritis such as Neuromyelitis Optica, Papilledema, Trigeminal Neuralgia, Vocal Cord Paralysis, Demyelinating Diseases such as Neuromyelitis Optica and Swayback, and Diabetic neuropathies such as diabetic foot.

[0662] Additional neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include nerve compression syndromes such as carpal tunnel syndrome, tarsal tunnel syndrome, thoracic outlet syndrome such as cervical rib syndrome, ulnar nerve compression syndrome, neuralgia such as causalgia, cervico-brachial neuralgia, facial neuralgia and trigeminal neuralgia, neuritis such as experimental-allergic neuritis, optic neuritis, polyneuritis, polyradiculoneuritis and radiculities such as polyradiculitis, hereditary motor and sensory neuropathies such as Charcot-Marie Disease, Hereditary Optic Atrophy, Refsum's Disease, Hereditary Spastic Paraplegia and Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies which include Congenital Analgesia and Familial Dysautonomia, POEMS Syndrome, Sciatica, Gustatory Sweating and Tetany).

### **Endocrine Disorders**

[0663] Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat, prevent, diagnose, and/or prognose disorders and/or diseases related to hormone imbalance, and/or disorders or diseases of the endocrine system.

[0664] Hormones secreted by the glands of the endocrine system control physical growth, sexual function, metabolism, and other functions. Disorders may be classified in two ways: disturbances in the production of hormones, and the inability of tissues to respond to hormones. The etiology of these hormone imbalance or endocrine system diseases, disorders or conditions may be genetic, somatic, such as cancer and some autoimmune diseases, acquired (e.g., by chemotherapy, injury or toxins), or infectious. Moreover, polynucleotides, polypeptides, antibodies, and/or agonists or antagonists of the present invention can be used as a marker or detector of a particular disease or disorder related to the endocrine system and/or hormone imbalance.

[0665] Endocrine system and/or hormone imbalance and/or diseases encompass disorders of uterine motility including, but not limited to: complications with pregnancy and labor (e.g., pre-term labor, post-term pregnancy, spontaneous abortion, and slow or stopped labor); and disorders and/or diseases of the menstrual cycle (e.g., dysmenorrhea and endometriosis).

[0666] Endocrine system and/or hormone imbalance disorders and/or diseases include disorders and/or diseases of the pancreas, such as, for example, diabetes mellitus, diabetes insipidus, congenital pancreatic agenesis, pheochromocytoma--islet cell tumor syndrome; disorders and/or diseases of the adrenal glands such as, for example, Addison's Disease, corticosteroid deficiency, virilizing disease, hirsutism, Cushing's Syndrome, hyperaldosteronism, pheochromocytoma; disorders and/or diseases of the pituitary gland, such as, for example, hyperpituitarism, hypopituitarism, pituitary dwarfism, pituitary adenoma, panhypopituitarism, acromegaly, gigantism; disorders and/or diseases of the thyroid, including but not limited to, hyperthyroidism, hypothyroidism, Plummer's disease, Graves' disease (toxic diffuse goiter), toxic nodular goiter, thyroiditis (Hashimoto's thyroiditis, subacute granulomatous thyroiditis, and silent lymphocytic thyroiditis), Pendred's syndrome, myxedema, cretinism, thyrotoxicosis, thyroid hormone coupling defect, thymic aplasia, Hurthle cell tumours of the thyroid, thyroid cancer, thyroid carcinoma, Medullary thyroid carcinoma; disorders and/or diseases of the parathyroid, such as, for example, hyperparathyroidism, hypoparathyroidism; disorders and/or diseases of the hypothalamus.

[0667] In addition, endocrine system and/or hormone imbalance disorders and/or diseases may also include disorders and/or diseases of the testes or ovaries, including cancer. Other disorders and/or diseases of the testes or ovaries further include, for example, ovarian cancer, polycystic ovary syndrome, Klinefelter's syndrome, vanishing testes syndrome (bilateral anorchia), congenital absence of Leydig's cells, cryptorchidism, Noonan's syndrome, myotonic dystrophy, capillary haemangioma of the testis (benign), neoplasias of the testis and neo-testis.

[0668] Moreover, endocrine system and/or hormone imbalance disorders and/or diseases may also include disorders and/or diseases such as, for example, polyglandular deficiency syndromes, pheochromocytoma, neuroblastoma, multiple Endocrine neoplasia, and disorders and/or cancers of endocrine tissues.

[0669] In another embodiment, a polypeptide of the invention, or polynucleotides, antibodies, agonists, or antagonists corresponding to that polypeptide, may be used to diagnose, prognose, prevent, and/or treat endocrine diseases and/or disorders associated with the tissue(s) in which the polypeptide of the invention is expressed, including one, two, three, four, five, or more tissues disclosed in Table 1, column 7 (Tissue Distribution Library Code).

### **Gastrointestinal Disorders**

[0670] Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat, prevent, diagnose, and/or prognose gastrointestinal disorders, including inflammatory diseases and/or conditions, infections, cancers (e.g., intestinal neoplasms (carcinoid tumor of the small intestine, non-Hodgkin's lymphoma of the small intestine, small bowel lymphoma)), and ulcers, such as peptic ulcers.

[0671] Gastrointestinal disorders include dysphagia, odynophagia, inflammation of the esophagus, peptic esophagitis, gastric reflux, submucosal fibrosis and stricturing, Mallory-Weiss lesions, leiomyomas, lipomas, epidermal cancers, adeoncarcinomas, gastric retention disorders, gastroenteritis, gastric atrophy, gastric/stomach cancers, polyps of the stomach, autoimmune disorders such as pernicious anemia, pyloric stenosis, gastritis (bacterial, viral, eosinophilic, stress-induced, chronic erosive, atrophic, plasma cell, and Ménétrier's), and peritoneal diseases (e.g., chyloperitoneum, hemoperitoneum,



mesenteric cyst, mesenteric lymphadenitis, mesenteric vascular occlusion, panniculitis, neoplasms, peritonitis, pneumoperitoneum, bubphrenic abscess).

[0672] Gastrointestinal disorders also include disorders associated with the small intestine, such as malabsorption syndromes, distension, irritable bowel syndrome, sugar intolerance, celiac disease, duodenal ulcers, duodenitis, tropical sprue, Whipple's disease, intestinal lymphangiectasia, Crohn's disease, appendicitis, obstructions of the ileum, Meckel's diverticulum, multiple diverticula, failure of complete rotation of the small and large intestine, lymphoma, and bacterial and parasitic diseases (such as Traveler's diarrhea, typhoid and paratyphoid, cholera, infection by Roundworms (*Ascariasis lumbricoides*), Hookworms (*Ancylostoma duodenale*), Threadworms (*Enterobius vermicularis*), Tapeworms (*Taenia saginata*, *Echinococcus granulosus*, *Diphyllobothrium spp.*, and *T. solium*).

[0673] Liver diseases and/or disorders include intrahepatic cholestasis (alagille syndrome, biliary liver cirrhosis), fatty liver (alcoholic fatty liver, reye syndrome), hepatic vein thrombosis, hepatolentricular degeneration, hepatomegaly, hepatopulmonary syndrome, hepatorenal syndrome, portal hypertension (esophageal and gastric varices), liver abscess (amebic liver abscess), liver cirrhosis (alcoholic, biliary and experimental), alcoholic liver diseases (fatty liver, hepatitis, cirrhosis), parasitic (hepatic echinococcosis, fascioliasis, amebic liver abscess), jaundice (hemolytic, hepatocellular, and cholestatic), cholestasis, portal hypertension, liver enlargement, ascites, hepatitis (alcoholic hepatitis, animal hepatitis, chronic hepatitis (autoimmune, hepatitis B, hepatitis C, hepatitis D, drug induced), toxic hepatitis, viral human hepatitis (hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E), Wilson's disease, granulomatous hepatitis, secondary biliary cirrhosis, hepatic encephalopathy, portal hypertension, varices, hepatic encephalopathy, primary biliary cirrhosis, primary sclerosing cholangitis, hepatocellular adenoma, hemangiomas, bile stones, liver failure (hepatic encephalopathy, acute liver failure), and liver neoplasms (angiomyolipoma, calcified liver metastases, cystic liver metastases, epithelial tumors, fibrolamellar hepatocarcinoma, focal nodular hyperplasia, hepatic adenoma, hepatobiliary cystadenoma, hepatoblastoma, hepatocellular carcinoma, hepatoma, liver cancer, liver hemangioendothelioma, mesenchymal hamartoma, mesenchymal tumors of liver, nodular regenerative hyperplasia, benign liver tumors

(Hepatic cysts [Simple cysts, Polycystic liver disease, Hepatobiliary cystadenoma, Choledochal cyst], Mesenchymal tumors [Mesenchymal hamartoma, Infantile hemangioendothelioma, Hemangioma, Peliosis hepatis, Lipomas, Inflammatory pseudotumor, Miscellaneous], Epithelial tumors [Bile duct epithelium (Bile duct hamartoma, Bile duct adenoma), Hepatocyte (Adenoma, Focal nodular hyperplasia, Nodular regenerative hyperplasia)], malignant liver tumors [hepatocellular, hepatoblastoma, hepatocellular carcinoma, cholangiocellular, cholangiocarcinoma, cystadenocarcinoma, tumors of blood vessels, angiosarcoma, Kaposi's sarcoma, hemangioendothelioma, other tumors, embryonal sarcoma, fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma, carcinosarcoma, teratoma, carcinoid, squamous carcinoma, primary lymphoma]), peliosis hepatis, erythrohepatic porphyria, hepatic porphyria (acute intermittent porphyria, porphyria cutanea tarda), Zellweger syndrome).

[0674] Pancreatic diseases and/or disorders include acute pancreatitis, chronic pancreatitis (acute necrotizing pancreatitis, alcoholic pancreatitis), neoplasms (adenocarcinoma of the pancreas, cystadenocarcinoma, insulinoma, gastrinoma, and glucagonoma, cystic neoplasms, islet-cell tumors, pancreoblastoma), and other pancreatic diseases (e.g., cystic fibrosis, cyst (pancreatic pseudocyst, pancreatic fistula, insufficiency)).

[0675] Gallbladder diseases include gallstones (cholelithiasis and choledocholithiasis), postcholecystectomy syndrome, diverticulosis of the gallbladder, acute cholecystitis, chronic cholecystitis, bile duct tumors, and mucocele.

[0676] Diseases and/or disorders of the large intestine include antibiotic-associated colitis, diverticulitis, ulcerative colitis, acquired megacolon, abscesses, fungal and bacterial infections, anorectal disorders (e.g., fissures, hemorrhoids), colonic diseases (colitis, colonic neoplasms [colon cancer, adenomatous colon polyps (e.g., villous adenoma), colon carcinoma, colorectal cancer], colonic diverticulitis, colonic diverticulosis, megacolon [Hirschsprung disease, toxic megacolon]; sigmoid diseases [proctocolitis, sigmoid neoplasms]), constipation, Crohn's disease, diarrhea (infantile diarrhea, dysentery), duodenal diseases (duodenal neoplasms, duodenal obstruction, duodenal ulcer, duodenitis), enteritis (enterocolitis), HIV enteropathy, ileal diseases (ileal neoplasms, ileitis), immunoproliferative small intestinal disease, inflammatory bowel

disease (ulcerative colitis, Crohn's disease), intestinal atresia, parasitic diseases (anisakiasis, balantidiasis, blastocystis infections, cryptosporidiosis, dientamoebiasis, amebic dysentery, giardiasis), intestinal fistula (rectal fistula), intestinal neoplasms (cecal neoplasms, colonic neoplasms, duodenal neoplasms, ileal neoplasms, intestinal polyps, jejunal neoplasms, rectal neoplasms), intestinal obstruction (afferent loop syndrome, duodenal obstruction, impacted feces, intestinal pseudo-obstruction [cecal volvulus, intussusception), intestinal perforation, intestinal polyps (colonic polyps, gardner syndrome, peutz-jeghers syndrome), jejunal diseases (jejunal neoplasms), malabsorption syndromes (blind loop syndrome, celiac disease, lactose intolerance, short bowel syndrome, tropical sprue, whipple's disease), mesenteric vascular occlusion, pneumatosis cystoides intestinalis, protein-losing enteropathies (intestinal lymphagiectasis), rectal diseases (anus diseases, fecal incontinence, hemorrhoids, proctitis, rectal fistula, rectal prolapse, rectocele), peptic ulcer (duodenal ulcer, peptic esophagitis, hemorrhage, perforation, stomach ulcer, Zollinger-Ellison syndrome), postgastrectomy syndromes (dumping syndrome), stomach diseases (e.g., achlorhydria, duodenogastric reflux (bile reflux), gastric antral vascular ectasia, gastric fistula, gastric outlet obstruction, gastritis (atrophic or hypertrophic), gastroparesis, stomach dilatation, stomach diverticulum, stomach neoplasms (gastric cancer, gastric polyps, gastric adenocarcinoma, hyperplastic gastric polyp), stomach rupture, stomach ulcer, stomach volvulus), tuberculosis, visceroptosis, vomiting (e.g., hematemesis, hyperemesis gravidarum, postoperative nausea and vomiting) and hemorrhagic colitis.

[0677] Further diseases and/or disorders of the gastrointestinal system include biliary tract diseases, such as, gastroschisis, fistula (e.g., biliary fistula, esophageal fistula, gastric fistula, intestinal fistula, pancreatic fistula), neoplasms (e.g., biliary tract neoplasms, esophageal neoplasms, such as adenocarcinoma of the esophagus, esophageal squamous cell carcinoma, gastrointestinal neoplasms, pancreatic neoplasms, such as adenocarcinoma of the pancreas, mucinous cystic neoplasm of the pancreas, pancreatic cystic neoplasms, pancreatoblastoma, and peritoneal neoplasms), esophageal disease (e.g., bullous diseases, candidiasis, glycogenic acanthosis, ulceration, barrett esophagus varices, atresia, cyst, diverticulum (e.g., Zenker's diverticulum), fistula (e.g., tracheoesophageal fistula), motility disorders (e.g., CREST syndrome, deglutition disorders, achalasia,

spasm, gastroesophageal reflux), neoplasms, perforation (e.g., Boerhaave syndrome, Mallory-Weiss syndrome), stenosis, esophagitis, diaphragmatic hernia (e.g., hiatal hernia); gastrointestinal diseases, such as, gastroenteritis (e.g., cholera morbus, norwalk virus infection), hemorrhage (e.g., hematemesis, melena, peptic ulcer hemorrhage), stomach neoplasms (gastric cancer, gastric polyps, gastric adenocarcinoma, stomach cancer)), hernia (e.g., congenital diaphragmatic hernia, femoral hernia, inguinal hernia, obturator hernia, umbilical hernia, ventral hernia), and intestinal diseases (e.g., cecal diseases (appendicitis, cecal neoplasms)).

#### **Developmental and Inherited Disorders**

[0678] Polynucleotides or polypeptides, or agonists or antagonists of the present invention may be used to treat, prevent, diagnose, and/or prognose diseases associated with mixed fetal tissues, including, but not limited to, developmental and inherited disorders or defects of the nervous system, musculoskeletal system, excretory system, cardiovascular system, hematopoietic system, gastrointestinal system, reproductive system, and respiratory system. Compositions of the present invention may also be used to treat, prevent, diagnose, and/or prognose developmental and inherited disorders or defects associated with, but not limited to, skin, hair, visual, and auditory tissues, metabolism. Additionally, the compositions of the invention may be useful in the diagnosis, treatment, and/or prevention of disorders or diseases associated with, but not limited to, chromosomal or genetic abnormalities and hyperproliferation or neoplasia.

[0679] Disorders or defects of the nervous system associated with developmental or inherited abnormalities that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, adrenoleukodystrophy, agenesis of corpus callosum, Alexander disease, anencephaly, Angelman syndrome, Arnold-Chiari deformity, Batten disease, Canavan disease, cephalic disorders, Charcot-Marie-Tooth disease, encephalocele, Friedreich's ataxia, Gaucher's disease, Gorlin syndrome, Hallervorden-Spatz disease, hereditary spastic paraplegia, Huntington disease, hydranencephaly, hydrocephalus, Joubert syndrome, Lesch-Nyhan syndrome, leukodystrophy, Menkes disease, microcephaly, Niemann-Pick Type C1, neurofibromatosis, porencephaly, progeria, proteus syndrome, Refsum disease, spina

bifida, Sturge-Weber syndrome, Tay-Sachs disease, tuberous sclerosis, and von Hippel-Lindau disease.

[0680] Developmental and inherited disorders resulting in disorders or defects of the musculoskeletal system that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, achondroplasia, atlanto-occipital fusion, arthrogryposis multiplex congenita, autosomal recessive muscular dystrophy, Becker's muscular dystrophy, cerebral palsy, choanal atresia, cleft lip, cleft palate, clubfoot, congenital amputation, congenital dislocation of the hip, congenital torticollis, congenital scoliosis, dopa-responsive dystonia, Duchenne muscular dystrophy, early-onset generalized dystonia, femoral torsion, Gorlin syndrome, hypophosphatasia, Klippel-Feil syndrome, knee dislocation, myoclonic dystonia, myotonic dystrophy, nail-patella syndrome, osteogenesis imperfecta, paroxysmal dystonia, progeria, prune-belly syndrome, rapid-onset dystonia parkinsonism, scoliosis, syndactyly, Treacher Collins' syndrome, velocardiofacial syndrome, and X-linked dystonia-parkinsonism.

[0681] Developmental or hereditary disorders or defects of the excretory system that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, Alport's syndrome, Bartter's syndrome, bladder diverticula, bladder exstrophy, cystinuria, epispadias, Fanconi's syndrome, Hartnup disease, horseshoe kidney, hypospadias, kidney agenesis, kidney ectopia, kidney malrotation, Liddle's syndrome, medullary cystic disease, medullary sponge, multicystic kidney, kidney polycystic kidney disease, nail-patella syndrome, Potter's syndrome, urinary tract flow obstruction, vitamin D-resistant rickets, and Wilm's tumor.

[0682] Cardiovascular disorders or defects of developmental or hereditary origin that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, aortic valve stenosis, atrial septal defects, arterioventricular (A-V) canal defect, bicuspid aortic valve, coarctation of the aorta, dextrocardia, Ebstein's anomaly, Eisenmenger's complex, hypoplastic left heart syndrome, Marfan syndrome, patent ductus arteriosus, progeria, pulmonary atresia, pulmonary valve stenosis, subaortic stenosis, tetralogy of fallot, total anomalous pulmonary venous (P-V) connection, transposition of the great arteries, tricuspid atresia, truncus arteriosus, ventricular septal defects. Developmental or inherited disorders resulting in disorders involving the

hematopoietic system that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but not limited to, Bernard-Soulier syndrome, Chédiak-Higashi syndrome, hemophilia, Hermansky-Pudlak syndrome, sickle cell anemia, storage pool disease, thromboxane A2 dysfunction, thrombasthenia, and von Willebrand's disease.

[0683] The compositions of the invention may also be used to diagnose, treat, and/or prevent developmental and inherited disorders resulting in disorders or defects of the gastrointestinal system, including, but not limited to, anal atresia, biliary atresia, esophageal atresia, diaphragmatic hernia, Hirschsprung's disease, Meckel's diverticulum, oligohydramnios, omphalocele, polyhydramnios, porphyria, situs inversus viscera. Developmental or inherited disorders resulting in metabolic disorders that may be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, alpha-1 antitrypsin deficiency, cystic fibrosis, hemochromatosis, lysosomal storage disease, phenylketonuria, Wilson's disease, and Zellweger syndrome.

[0684] Disorders of the reproductive system that are developmentally or hereditary related that may also be diagnosed, treated, and/or prevented with the compositions of the invention include, but are not limited to, androgen insensitivity syndrome, ambiguous genitalia, autosomal sex reversal, congenital adrenale hyperplasia, gonadoblastoma, ovarian germ cell cancer, pseudohermaphroditism, true hermaphroditism, undescended testis, XX male syndrome, and XY female type gonadal dysgenesis. The compositions of the invention may also be used to diagnose, treat, and/or prevent developmental or inherited respiratory defects including, but not limited to, askin tumor, azygos lobe, congenital diaphragmatic hernia, congenital lobar emphysema, cystic adenomatoid malformation, lobar emphysema, hyaline membrane disease, and pectus excavatum.

[0685] Developmental or inherited disorders may also result from chromosomal or genetic aberration that may be diagnosed, treated, and/or prevented with the compositions of the invention including, but not limited to, 4p- syndrome, cri du chat syndrome, Digeorge syndrome, Down's syndrome, Edward's syndrome, fragile X syndrome, Klinefelter's syndrome, Patau's syndrome, Prader-Willi syndrome, progeria, Turner's syndrome, triple X syndrome, and XYY syndrome. Other developmental disorders that can be diagnosed, treated, and/or prevented with the compositions of the invention,

include, but are not limited to, fetal alcohol syndrome, and can be caused by environmental factors surrounding the developing fetus.

[0686] The compositions of the invention may further be able to be used to diagnose, treat, and/or prevent errors in development or a genetic disposition that may result in hyperproliferative disorders or neoplasms, including, but not limited to, acute childhood lymphoblastic leukemia, askin tumor, Beckwith-Wiedemann syndrome, childhood acute myeloid leukemia, childhood brain stem glioma, childhood cerebellar astrocytoma, childhood extracranial germ cell tumors childhood (primary), gonadoblastoma, hepatocellular cancer, childhood Hodgkin's disease, childhood Hodgkin's lymphoma, childhood hypothalamic and visual pathway glioma, childhood (primary) liver cancer, childhood lymphoblastic leukemia, childhood medulloblastoma, childhood non-Hodgkin's lymphoma, childhood pineal and supratentorial primitive neuroectodermal tumors, childhood primary liver cancer, childhood rhabdomyosarcoma, childhood soft tissue sarcoma, Gorlin syndrome, familial multiple endocrine neoplasia type I, neuroblastoma, ovarian germ cell cancer, pheochromocytoma, retinoblastoma, and Wilm's tumor.

[0687] Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators, gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppository solid pharmaceutical formulations, decanting or topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

#### **Diseases at the Cellular Level**

[0688] Diseases associated with increased cell survival or the inhibition of apoptosis that could be treated, prevented, diagnosed and/or prognosed using polynucleotides or polypeptides, as well as antagonists or agonists of the present invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac

tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection.

[0689] In preferred embodiments, polynucleotides, polypeptides, and/or antagonists of the invention are used to inhibit growth, progression, and/or metastasis of cancers, in particular those [listed above] involving breast and ovarian tissues.

[0690] Additional diseases or conditions associated with increased cell survival that could be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer,



testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, and retinoblastoma.

[0691] Diseases associated with increased apoptosis that could be treated, prevented, diagnosed, and/or prognosed using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, include, but are not limited to, AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury); liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestasis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

#### **Wound Healing and Epithelial Cell Proliferation**

[0692] In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate epithelial cell proliferation and basal keratinocytes for the purpose of wound healing, and to stimulate hair follicle production and healing of dermal wounds. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may be clinically useful in stimulating wound healing including surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and

antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote dermal reestablishment subsequent to dermal loss.

[0693] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to increase the adherence of skin grafts to a wound bed and to stimulate re-epithelialization from the wound bed. The following are types of grafts that polynucleotides or polypeptides, agonists or antagonists of the present invention, could be used to increase adherence to a wound bed: autografts, artificial skin, allografts, autodermic graft, autoepidermic grafts, avascular grafts, Blair-Brown grafts, bone graft, brephoplastic grafts, cutis graft, delayed graft, dermic graft, epidermic graft, fascia graft, full thickness graft, heterologous graft, xenograft, homologous graft, hyperplastic graft, lamellar graft, mesh graft, mucosal graft, Ollier-Thiersch graft, omentopial graft, patch graft, pedicle graft, penetrating graft, split skin graft, thick split graft. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, can be used to promote skin strength and to improve the appearance of aged skin.

[0694] It is believed that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, will also produce changes in hepatocyte proliferation, and epithelial cell proliferation in the lung, breast, pancreas, stomach, small intestine, and large intestine. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could promote proliferation of epithelial cells such as sebocytes, hair follicles, hepatocytes, type II pneumocytes, mucin-producing goblet cells, and other epithelial cells and their progenitors contained within the skin, lung, liver, and gastrointestinal tract. Polynucleotides or polypeptides, agonists or antagonists of the present invention, may promote proliferation of endothelial cells, keratinocytes, and basal keratinocytes.

[0695] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to reduce the side effects of gut toxicity that result from radiation, chemotherapy treatments or viral infections. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may have a cytoprotective effect on the small intestine mucosa. Polynucleotides or polypeptides, as

well as agonists or antagonists of the present invention, may also stimulate healing of mucositis (mouth ulcers) that result from chemotherapy and viral infections.

[0696] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could further be used in full regeneration of skin in full and partial thickness skin defects, including burns, (i.e., repopulation of hair follicles, sweat glands, and sebaceous glands), treatment of other skin defects such as psoriasis. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat epidermolysis bullosa, a defect in adherence of the epidermis to the underlying dermis which results in frequent, open and painful blisters by accelerating reepithelialization of these lesions. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to treat gastric and duodenal ulcers and help heal by scar formation of the mucosal lining and regeneration of glandular mucosa and duodenal mucosal lining more rapidly. Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, are diseases, which result in destruction of the mucosal surface of the small or large intestine, respectively. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote the resurfacing of the mucosal surface to aid more rapid healing and to prevent progression of inflammatory bowel disease. Treatment with polynucleotides or polypeptides, agonists or antagonists of the present invention, is expected to have a significant effect on the production of mucus throughout the gastrointestinal tract and could be used to protect the intestinal mucosa from injurious substances that are ingested or following surgery. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat diseases associate with the under expression.

[0697] Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to prevent and heal damage to the lungs due to various pathological states. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could stimulate proliferation and differentiation and promote the repair of alveoli and bronchiolar epithelium to prevent or treat acute or chronic lung damage. For example, emphysema, which results in the progressive loss of aveoli, and inhalation injuries, i.e., resulting from smoke inhalation and

burns, that cause necrosis of the bronchiolar epithelium and alveoli could be effectively treated using polynucleotides or polypeptides, agonists or antagonists of the present invention. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to stimulate the proliferation of and differentiation of type II pneumocytes, which may help treat or prevent disease such as hyaline membrane diseases, such as infant respiratory distress syndrome and bronchopulmonary dysplasia, in premature infants.

[0698] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could stimulate the proliferation and differentiation of hepatocytes and, thus, could be used to alleviate or treat liver diseases and pathologies such as fulminant liver failure caused by cirrhosis, liver damage caused by viral hepatitis and toxic substances (i.e., acetaminophen, carbon tetrachloride and other hepatotoxins known in the art).

In addition, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to maintain the islet function so as to alleviate, delay or prevent permanent manifestation of the disease. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used as an auxiliary in islet cell transplantation to improve or promote islet cell function.

### **Infectious Disease**

[0699] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

[0700] Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention. Examples of viruses, include, but are not limited to Examples of viruses, include, but are not limited to the following DNA and RNA viruses and viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Dengue, EBV, HIV, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza A, Influenza B, and parainfluenza), Papilloma virus, Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiolitis, respiratory syncytial virus, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), Japanese B encephalitis, Junin, Chikungunya, Rift Valley fever, yellow fever, meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat: meningitis, Dengue, EBV, and/or hepatitis (e.g., hepatitis B). In an additional specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat patients nonresponsive to one or more other commercially available hepatitis vaccines. In a further specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat AIDS.

[0701] Similarly, bacterial and fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, the following Gram-Negative and Gram-positive bacteria, bacterial families, and fungi: Actinomyces (e.g.,

Nocardia), Acinetobacter, *Cryptococcus neoformans*, Aspergillus, Bacillaceae (e.g., *Bacillus anthracis*), Bacteroides (e.g., *Bacteroides fragilis*), Blastomycosis, Bordetella, Borrelia (e.g., *Borrelia burgdorferi*), Brucella, Candidia, Campylobacter, Chlamydia, Clostridium (e.g., *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Clostridium tetani*), Coccidioides, Corynebacterium (e.g., *Corynebacterium diphtheriae*), Cryptococcus, Dermatocycoses, *E. coli* (e.g., Enterotoxigenic *E. coli* and Enterohemorrhagic *E. coli*), Enterobacter (e.g. *Enterobacter aerogenes*), Enterobacteriaceae (Klebsiella, Salmonella (e.g., *Salmonella typhi*, *Salmonella enteritidis*, *Salmonella typhi*), Serratia, Yersinia, Shigella), Erysipelothrix, Haemophilus (e.g., *Haemophilus influenza* type B), Helicobacter, Legionella (e.g., *Legionella pneumophila*), Leptospira, Listeria (e.g., *Listeria monocytogenes*), Mycoplasma, Mycobacterium (e.g., *Mycobacterium leprae* and *Mycobacterium tuberculosis*), Vibrio (e.g., *Vibrio cholerae*), Neisseriaceae (e.g., *Neisseria gonorrhea*, *Neisseria meningitidis*), Pasteurellaceae, Proteus, Pseudomonas (e.g., *Pseudomonas aeruginosa*), Rickettsiaceae, Spirochetes (e.g., Treponema spp., Leptospira spp., Borrelia spp.), Shigella spp., Staphylococcus (e.g., *Staphylococcus aureus*), Meningiococcus, Pneumococcus and Streptococcus (e.g., *Streptococcus pneumoniae* and Groups A, B, and C Streptococci), and Ureaplasmas. These bacterial, parasitic, and fungal families can cause diseases or symptoms, including but not limited to: antibiotic-resistant infections, bacteremia, endocarditis, septicemia, eye infections (e.g., conjunctivitis), uveitis, tuberculosis, gingivitis, bacterial diarrhea, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, dental caries, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, dysentery, paratyphoid fever, food poisoning, Legionella disease, chronic and acute inflammation, erythema, yeast infections, typhoid, pneumonia, gonorrhea, meningitis (e.g., meningitis types A and B), chlamydia, syphilis, diphtheria, leprosy, brucellosis, peptic ulcers, anthrax, spontaneous abortions, birth defects, pneumonia, lung infections, ear infections, deafness, blindness, lethargy, malaise, vomiting, chronic diarrhea, Crohn's disease, colitis, vaginosis, sterility, pelvic inflammatory diseases, candidiasis, paratuberculosis, tuberculosis, lupus, botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses),

toxemia, urinary tract infections, wound infections, noscomial infections. Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, agonists or antagonists of the invention are used to treat: tetanus, diphtheria, botulism, and/or meningitis type B.

[0702] Moreover, parasitic agents causing disease or symptoms that can be treated, prevented, and/or diagnosed by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, the following families or class: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Schistosoma, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas and Sporozoans (e.g., *Plasmodium virax*, *Plasmodium falciparum*, *Plasmodium malariae* and *Plasmodium ovale*). These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), malaria, pregnancy complications, and toxoplasmosis. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat, prevent, and/or diagnose any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat, prevent, and/or diagnose malaria.

[0703] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

#### Regeneration

[0704] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues,

could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

[0705] Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vasculature (including vascular and lymphatics), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

[0706] Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

[0707] Similarly, nerve and brain tissue could also be regenerated by using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotides or polypeptides, as well as agonists or antagonists of the present invention.



**Chemotaxis**

[0708] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may have chemotaxis activity. A chemotaxic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

[0709] Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may increase chemotaxic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotaxic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

[0710] It is also contemplated that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could be used as an inhibitor of chemotaxis.

**Binding Activity**

[0711] A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

[0712] Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5